WEBVTT

NOTE duration:"00:59:29"

NOTE recognizability:0.757

NOTE language:en-us

NOTE Confidence: 0.914125553636364

00:00:00.000 --> 00:00:04.272 OK. Good afternoon and welcome to

NOTE Confidence: 0.914125553636364

00:00:04.272 --> 00:00:08.500 today's grand rounds in pathology.

NOTE Confidence: 0.914125553636364

 $00:00:08.500 \rightarrow 00:00:12.595$ I would like to introduce today's speaker,

NOTE Confidence: 0.914125553636364

00:00:12.600 -> 00:00:14.538 doctor Patricia Dossantos.

NOTE Confidence: 0.914125553636364

 $00{:}00{:}14.538 \dashrightarrow 00{:}00{:}18.372$ A professor and associate chair of

NOTE Confidence: 0.914125553636364

00:00:18.372 --> 00:00:21.878 chemistry from Wake Forest University.

NOTE Confidence: 0.914125553636364

 $00{:}00{:}21.880 \dashrightarrow 00{:}00{:}24.196$ Patricia received her bachelor's

NOTE Confidence: 0.914125553636364

 $00{:}00{:}24.196 \dashrightarrow 00{:}00{:}27.670$ at the Federal University of Rio

NOTE Confidence: 0.914125553636364

00:00:27.767 --> 00:00:30.418 Grande in Porto Alegre, Brazil.

NOTE Confidence: 0.914125553636364

00:00:30.418 --> 00:00:35.940 And then came to the United States to do

NOTE Confidence: 0.914125553636364

 $00{:}00{:}35{.}940 \dashrightarrow 00{:}00{:}39{.}790$ a PhD in biochemistry at Virginia Tech.

NOTE Confidence: 0.914125553636364

 $00{:}00{:}39.790 \dashrightarrow 00{:}00{:}41.906$ After completing her PhD,

NOTE Confidence: 0.914125553636364

 $00{:}00{:}41.906 \dashrightarrow 00{:}00{:}44.618$ she stayed at Virginia Tech for

 $00:00:44.618 \rightarrow 00:00:47.457$ three years as a postdoc associate.

NOTE Confidence: 0.914125553636364

 $00{:}00{:}47.460 \dashrightarrow 00{:}00{:}49.560$ And was then recruited to the

NOTE Confidence: 0.914125553636364

00:00:49.560 --> 00:00:51.982 Department of Chemistry at Wake Forest

NOTE Confidence: 0.914125553636364

 $00:00:51.982 \rightarrow 00:00:53.898$ University as assistant professor,

NOTE Confidence: 0.914125553636364

 $00:00:53.900 \rightarrow 00:00:56.570$ where she very quickly wrote through

NOTE Confidence: 0.914125553636364

 $00:00:56.570 \longrightarrow 00:00:59.387$ rose through the ranks to full

NOTE Confidence: 0.914125553636364

 $00:00:59.387 \dashrightarrow 00:01:01.299$ professor and associate chair.

NOTE Confidence: 0.914125553636364

 $00:01:01.300 \rightarrow 00:01:03.920$ Throughout her academic development,

NOTE Confidence: 0.914125553636364

 $00:01:03.920 \rightarrow 00:01:07.195$ Patricia has always been outstanding.

NOTE Confidence: 0.914125553636364

 $00:01:07.200 \rightarrow 00:01:11.117$ In the year she graduated with her doctorate,

NOTE Confidence: 0.914125553636364

00:01:11.117 $\operatorname{-->}$ 00:01:13.212 she received the Outstanding Graduate

NOTE Confidence: 0.914125553636364

00:01:13.212 --> 00:01:15.120 Student Award at Virginia Tech,

NOTE Confidence: 0.914125553636364

 $00{:}01{:}15{.}120 \dashrightarrow 00{:}01{:}18{.}858$ and she was also the commencement speaker

NOTE Confidence: 0.914125553636364

00:01:18.858 --> 00:01:22.907 at the graduation ceremony at Virginia Tech.

NOTE Confidence: 0.914125553636364

 $00:01:22.910 \dashrightarrow 00:01:26.123$ She further received at Wake Forest the

NOTE Confidence: 0.914125553636364

00:01:26.123 --> 00:01:28.710 faculty Excellence in Research award,

 $00:01:28.710 \longrightarrow 00:01:31.040$ the Robert Depth and Deborah

NOTE Confidence: 0.914125553636364

00:01:31.040 --> 00:01:32.904 Lee Faculty Fellowship Award,

NOTE Confidence: 0.914125553636364

 $00:01:32.910 \dashrightarrow 00:01:35.640$ and the Eureka Faculty Award of

NOTE Confidence: 0.914125553636364

 $00:01:35.640 \rightarrow 00:01:38.240$ Excellence in Mentoring and Research.

NOTE Confidence: 0.914125553636364

00:01:38.240 --> 00:01:40.964 Patricia has published over 60 peer

NOTE Confidence: 0.914125553636364

 $00:01:40.964 \dashrightarrow 00:01:43.540$ reviewed papers and book chapters,

NOTE Confidence: 0.914125553636364

 $00{:}01{:}43.540 \dashrightarrow 00{:}01{:}46.823$ she's an editor in methods in molecular

NOTE Confidence: 0.914125553636364

 $00:01:46.823 \rightarrow 00:01:49.734$ biology and she has had close to

NOTE Confidence: 0.914125553636364

 $00:01:49.734 \longrightarrow 00:01:52.176$ 150 invited talks and peer reviewed

NOTE Confidence: 0.914125553636364

 $00:01:52.176 \rightarrow 00:01:55.000$ posters and platform presentations at

NOTE Confidence: 0.914125553636364

 $00:01:55.000 \rightarrow 00:01:57.576$ national and international meetings.

NOTE Confidence: 0.914125553636364

00:01:57.580 --> 00:02:01.413 She has been funded by two grants from

NOTE Confidence: 0.914125553636364

 $00{:}02{:}01{.}413 \dashrightarrow 00{:}02{:}04{.}479$ by the National Science Foundation and

NOTE Confidence: 0.914125553636364

 $00{:}02{:}04.479 \dashrightarrow 00{:}02{:}07.409$ has interdisciplinary research grants

NOTE Confidence: 0.914125553636364

 $00:02:07.409 \rightarrow 00:02:12.053$ from the North Carolina Biotechnology Center.

00:02:12.060 --> 00:02:13.866 In addition to her excellent science,

NOTE Confidence: 0.914125553636364

00:02:13.870 --> 00:02:17.070 Patricia is a extremely successful

NOTE Confidence: 0.914125553636364

 $00:02:17.070 \longrightarrow 00:02:18.990$ teacher and mentor.

NOTE Confidence: 0.914125553636364

 $00:02:18.990 \rightarrow 00:02:21.415$ She teaches 6 biochemistry courses

NOTE Confidence: 0.914125553636364

 $00{:}02{:}21.415 \dashrightarrow 00{:}02{:}22.870$ at Wake Forest.

NOTE Confidence: 0.914125553636364

 $00{:}02{:}22{.}870 \dashrightarrow 00{:}02{:}28{.}194$ She has mentored 20 PhD students

NOTE Confidence: 0.914125553636364

 $00:02:28.194 \longrightarrow 00:02:30.567$ and honor students.

NOTE Confidence: 0.914125553636364

 $00:02:30.570 \dashrightarrow 00:02:34.385$ She has also mentored 10 postdoc Fellows,

NOTE Confidence: 0.914125553636364

 $00{:}02{:}34{.}390 \dashrightarrow 00{:}02{:}38{.}632$ and she has a fantastic track record

NOTE Confidence: 0.914125553636364

 $00:02:38.632 \rightarrow 00:02:41.420$ of mentoring undergraduate students.

NOTE Confidence: 0.914125553636364

 $00{:}02{:}41{.}420 \dashrightarrow 00{:}02{:}43{.}975$ Who do their honour research

NOTE Confidence: 0.914125553636364

 $00{:}02{:}43.975 \dashrightarrow 00{:}02{:}46.019$ thesis in her lab.

NOTE Confidence: 0.914125553636364

 $00:02:46.020 \longrightarrow 00:02:49.835$ So she has mentored over 60 of

NOTE Confidence: 0.914125553636364

 $00:02:49.835 \longrightarrow 00:02:51.470$ these undergraduate students.

NOTE Confidence: 0.914125553636364

 $00:02:51.470 \longrightarrow 00:02:53.014$ Outside of Wake Forest,

NOTE Confidence: 0.914125553636364

 $00:02:53.014 \rightarrow 00:02:55.640$ she is a reviewer on standing

- NOTE Confidence: 0.914125553636364
- 00:02:55.640 --> 00:02:57.800 review panels for NIH,

00:02:57.800 --> 00:02:58.976 National Science Foundation

NOTE Confidence: 0.914125553636364

00:02:58.976 --> 00:03:00.936 and the Department of Energy.

NOTE Confidence: 0.914125553636364

 $00:03:00.940 \longrightarrow 00:03:03.670$ She has been a session chair at

NOTE Confidence: 0.914125553636364

 $00{:}03{:}03{.}670 \dashrightarrow 00{:}03{:}05{.}930$ Gordon Conferences and a session

NOTE Confidence: 0.914125553636364

 $00{:}03{:}05{.}930 \dashrightarrow 00{:}03{:}07{.}954$ chair at International Conference

NOTE Confidence: 0.914125553636364

 $00:03:07.954 \longrightarrow 00:03:09.978$ for iron sulfide clusters.

NOTE Confidence: 0.914125553636364

 $00:03:09.980 \rightarrow 00:03:13.641$ She's an epoch reviewer for many national

NOTE Confidence: 0.914125553636364

 $00:03:13.641 \rightarrow 00:03:16.000$ and international funding agencies.

NOTE Confidence: 0.914125553636364

00:03:16.000 - 00:03:19.408 Her talk today is entitled The

NOTE Confidence: 0.914125553636364

00:03:19.408 --> 00:03:22.276 Synthesis and Dynamic Landscape of

NOTE Confidence: 0.914125553636364

00:03:22.276 --> 00:03:23.587 Transfer RNA's Epic transcriptome

NOTE Confidence: 0.914125553636364

 $00{:}03{:}23.587 \dashrightarrow 00{:}03{:}25.959$ and I think we are in for a treat,

NOTE Confidence: 0.914125553636364

 $00:03:25.960 \dashrightarrow 00:03:28.470$ so please welcome Patricia Dossantos.

NOTE Confidence: 0.832084448333333

 $00{:}03{:}33{.}330 \dashrightarrow 00{:}03{:}36{.}345$ Thanks for the kind introduction

 $00:03:36.345 \longrightarrow 00:03:38.718$ and invitation to come here.

NOTE Confidence: 0.832084448333333

 $00:03:38.718 \longrightarrow 00:03:41.370$ I had a really great time.

NOTE Confidence: 0.832084448333333

 $00:03:41.370 \rightarrow 00:03:43.410$ Today very special meeting and

NOTE Confidence: 0.832084448333333

00:03:43.410 - > 00:03:45.450 talking about women in academia.

NOTE Confidence: 0.832084448333333

 $00:03:45.450 \longrightarrow 00:03:47.522$ Really enjoyed that with

NOTE Confidence: 0.832084448333333

 $00{:}03{:}47.522 \dashrightarrow 00{:}03{:}48.558$ department colleagues.

NOTE Confidence: 0.941259797

00:03:50.800 --> 00:03:54.960 OK. So what I want to share with you today,

NOTE Confidence: 0.941259797

00:03:54.960 --> 00:03:58.257 it's my work on T RNA modification.

NOTE Confidence: 0.941259797

 $00{:}03{:}58.260 \dashrightarrow 00{:}04{:}01.732$ So in changes on T RNA modifications

NOTE Confidence: 0.941259797

 $00:04:01.732 \longrightarrow 00:04:04.738$ and how that has an impact,

NOTE Confidence: 0.941259797

00:04:04.740 --> 00:04:07.304 but before I do that kind of

NOTE Confidence: 0.941259797

 $00:04:07.304 \longrightarrow 00:04:10.760$ like very broad, we know that.

NOTE Confidence: 0.941259797

 $00:04:10.760 \dashrightarrow 00:04:12.110$ Several biochemical reactions,

NOTE Confidence: 0.941259797

 $00:04:12.110 \longrightarrow 00:04:15.260$ they rely on the chemistry afforded by

NOTE Confidence: 0.941259797

 $00{:}04{:}15.332 \dashrightarrow 00{:}04{:}18.110$ protein cofactors and then the enzymes

NOTE Confidence: 0.941259797

 $00:04:18.110 \dashrightarrow 00:04:19.962$ associated with those cofactors.

- NOTE Confidence: 0.941259797
- $00{:}04{:}19{.}970 \dashrightarrow 00{:}04{:}21{.}758$ So among those cofactors,
- NOTE Confidence: 0.941259797
- 00:04:21.758 --> 00:04:23.993 sulfur containing cofactors are widely
- NOTE Confidence: 0.941259797
- $00{:}04{:}23.993 \dashrightarrow 00{:}04{:}26.586$ distributed in nature and then they are
- NOTE Confidence: 0.941259797
- $00:04:26.586 \rightarrow 00:04:28.390$ actually participate in several lives.
- NOTE Confidence: 0.941259797
- 00:04:28.390 --> 00:04:31.606 Sustaining reactions like photosynthesis,
- NOTE Confidence: 0.941259797
- $00:04:31.606 \rightarrow 00:04:34.546$ respiration, Nigel fixation will not
- NOTE Confidence: 0.941259797
- $00:04:34.546 \longrightarrow 00:04:37.750$ be here today without those processes.
- NOTE Confidence: 0.941259797
- $00:04:37.750 \longrightarrow 00:04:41.575$ So the main purpose of my lab is really.
- NOTE Confidence: 0.941259797
- $00:04:41.580 \longrightarrow 00:04:44.370$ Trying to understand.
- NOTE Confidence: 0.941259797
- $00:04:44.370 \longrightarrow 00:04:46.680$ Chemical futures for the synthesis
- NOTE Confidence: 0.941259797
- 00:04:46.680 --> 00:04:48.528 of sulfur containing cofactors,
- NOTE Confidence: 0.941259797
- $00{:}04{:}48.530 \dashrightarrow 00{:}04{:}50.120$ which are some of the molecules
- NOTE Confidence: 0.941259797
- $00:04:50.120 \longrightarrow 00:04:51.610$ shown here on this screen,
- NOTE Confidence: 0.941259797
- $00{:}04{:}51.610 \dashrightarrow 00{:}04{:}53.890$ and so scientists and the
- NOTE Confidence: 0.941259797
- $00:04:53.890 \longrightarrow 00:04:56.170$ function of those four factors,
- NOTE Confidence: 0.941259797

 $00:04:56.170 \longrightarrow 00:04:58.450$ so relevant for today's talk,

NOTE Confidence: 0.941259797

 $00:04:58.450 \dashrightarrow 00:05:03.550$ is the synthesis of Taiwan nucleosides.

NOTE Confidence: 0.941259797

 $00:05:03.550 \longrightarrow 00:05:04.930$ You see them out, yeah.

NOTE Confidence: 0.941259797

 $00{:}05{:}04{.}930 \dashrightarrow 00{:}05{:}06{.}414$ So Tyrone nucleosides that

NOTE Confidence: 0.941259797

 $00:05:06.414 \longrightarrow 00:05:08.640$ are present on to your RNA.

NOTE Confidence: 0.585111253333333

00:05:10.660 --> 00:05:13.588 So T RNA has, you know,

NOTE Confidence: 0.585111253333333

 $00:05:13.590 \rightarrow 00:05:16.320$ very well known function as serving

NOTE Confidence: 0.585111253333333

 $00:05:16.320 \longrightarrow 00:05:19.330$ as a dactyl in translation.

NOTE Confidence: 0.585111253333333

 $00{:}05{:}19{.}330 \dashrightarrow 00{:}05{:}22{.}730$ Granada reacts with a minoacyl tyranny

NOTE Confidence: 0.585111253333333

 $00{:}05{:}22.730 \dashrightarrow 00{:}05{:}26.328$ synthetase for the attachment of a mino

NOTE Confidence: 0.585111253333333

00:05:26.328 --> 00:05:29.401 acids to their cognate T RNA molecules NOTE Confidence: 0.585111253333333

 $00:05:29.401 \dashrightarrow 00:05:32.607$ which are then brought to the ribosome NOTE Confidence: 0.585111253333333

 $00{:}05{:}32{.}607 \dashrightarrow 00{:}05{:}35{.}798$ at the ribosomes tier and a interact

NOTE Confidence: 0.585111253333333

 $00{:}05{:}35{.}798 \dashrightarrow 00{:}05{:}38{.}412$ with the messenger RNA enabling the

NOTE Confidence: 0.585111253333333

 $00{:}05{:}38{.}412 \dashrightarrow 00{:}05{:}40{.}998$ translation of the genetic code and

NOTE Confidence: 0.585111253333333

 $00:05:40.998 \rightarrow 00:05:44.599$ the by doing so they promote peptide

- NOTE Confidence: 0.585111253333333
- $00:05:44.599 \rightarrow 00:05:46.723$ synthesis or protein synthesis.
- NOTE Confidence: 0.585111253333333
- $00:05:46.730 \rightarrow 00:05:49.690$ What most people don't know is that tyranny.
- NOTE Confidence: 0.585111253333333
- 00:05:49.690 --> 00:05:51.618 One, no canonical role,
- NOTE Confidence: 0.585111253333333
- $00:05:51.618 \rightarrow 00:05:54.950$ so like several roles in Atable ISM,
- NOTE Confidence: 0.585111253333333
- $00:05:54.950 \longrightarrow 00:05:56.276$ so tyranny molecules,
- NOTE Confidence: 0.585111253333333
- $00{:}05{:}56{.}276 \dashrightarrow 00{:}05{:}59{.}370$ they have an impact on gene regulation.
- NOTE Confidence: 0.585111253333333
- $00:05:59.370 \rightarrow 00:06:02.210$ They are also able to sense nutrient sensing.
- NOTE Confidence: 0.585111253333333
- $00:06:02.210 \dashrightarrow 00:06:04.044$ So the relevant to the story that
- NOTE Confidence: 0.585111253333333
- $00{:}06{:}04.044 \dashrightarrow 00{:}06{:}06.088$ I'm going to share with you today,
- NOTE Confidence: 0.585111253333333
- $00:06:06.090 \longrightarrow 00:06:08.505$ they are mediate a seller
- NOTE Confidence: 0.585111253333333
- $00:06:08.505 \longrightarrow 00:06:09.954$ and stress responses.
- NOTE Confidence: 0.585111253333333
- 00:06:09.960 --> 00:06:13.026 They can sense UV radiation and
- NOTE Confidence: 0.585111253333333
- $00{:}06{:}13.026 \dashrightarrow 00{:}06{:}14.559$ modulate translational capacity.
- NOTE Confidence: 0.585111253333333
- 00:06:14.560 --> 00:06:17.806 Under those conditions T RNA is
- NOTE Confidence: 0.585111253333333
- $00:06:17.806 \rightarrow 00:06:19.970$ important for viral replication.
- NOTE Confidence: 0.585111253333333

 $00:06:19.970 \longrightarrow 00:06:22.316$ So the example here is that

NOTE Confidence: 0.585111253333333

00:06:22.320 --> 00:06:24.770 modified T RNA actually assists

NOTE Confidence: 0.585111253333333

 $00:06:24.770 \longrightarrow 00:06:27.220$ replication of the HIV virus.

NOTE Confidence: 0.585111253333333

 $00:06:27.220 \longrightarrow 00:06:29.375$ And they're involved in other

NOTE Confidence: 0.585111253333333

 $00{:}06{:}29{.}375 \dashrightarrow 00{:}06{:}31{.}530$ functions in addition to the

NOTE Confidence: 0.585111253333333

 $00:06:31.610 \rightarrow 00:06:34.140$ roles of intact tyranny molecules.

NOTE Confidence: 0.585111253333333

 $00{:}06{:}34.140 \dashrightarrow 00{:}06{:}36.359$ In all these processes that I described

NOTE Confidence: 0.585111253333333

 $00:06:36.359 \rightarrow 00:06:38.532$ to you, fragments of tyranny a,

NOTE Confidence: 0.585111253333333

 $00{:}06{:}38.532 \dashrightarrow 00{:}06{:}40.447$ there are also equally important

NOTE Confidence: 0.585111253333333

00:06:40.447 --> 00:06:43.000 in metabolism. They are involved.

NOTE Confidence: 0.585111253333333

 $00:06:43.000 \dashrightarrow 00:06:45.300$ They sell proliferation in cancer,

NOTE Confidence: 0.585111253333333

 $00{:}06{:}45{.}300 \dashrightarrow 00{:}06{:}47{.}452$ it hosts defense mechanisms.

NOTE Confidence: 0.585111253333333

 $00:06:47.452 \rightarrow 00:06:51.766$ So fragments of that tyranny is not only

NOTE Confidence: 0.585111253333333

 $00:06:51.766 \rightarrow 00:06:54.730$ by products of degradation of T RNA.

NOTE Confidence: 0.585111253333333

 $00{:}06{:}54{.}730 \dashrightarrow 00{:}06{:}55{.}685$ Uh.

NOTE Confidence: 0.585111253333333

 $00:06:55.685 \longrightarrow 00:06:56.640$ So.

 $00:07:27.670 \longrightarrow 00:07:28.750$ The consequences?

NOTE Confidence: 0.84068186444444

00:07:31.580 --> 00:07:34.982 OK. I'll keep going for those of you there.

NOTE Confidence: 0.6782445425

00:07:38.870 --> 00:07:41.789 Read tyranny modifications

NOTE Confidence: 0.6782445425

 $00:07:41.789 \dashrightarrow 00:07:45.036$ reported into biological TRN's.

NOTE Confidence: 0.6782445425

 $00{:}07{:}45.036 \dashrightarrow 00{:}07{:}47.318$ So in the human genome there are

NOTE Confidence: 0.6782445425

 $00{:}07{:}47.318 \dashrightarrow 00{:}07{:}49.529$ many T RNA genes and then we

NOTE Confidence: 0.6782445425

 $00{:}07{:}49.529 \dashrightarrow 00{:}07{:}51.866$ what we know is that ternative is

NOTE Confidence: 0.6782445425

 $00:07:51.866 \longrightarrow 00:07:54.182$ found in the cytoplasm and called

NOTE Confidence: 0.6782445425

 $00{:}07{:}54.182 \dashrightarrow 00{:}07{:}56.733$ by nuclear genomic information.

NOTE Confidence: 0.6782445425

 $00:07:56.733 \longrightarrow 00:07:58.896$ It's also modified.

NOTE Confidence: 0.6782445425

00:07:58.900 --> 00:08:01.006 So while the structure of tyranny

NOTE Confidence: 0.6782445425

 $00{:}08{:}01{.}006 \dashrightarrow 00{:}08{:}02{.}818$ and then another subset of

NOTE Confidence: 0.6782445425

 $00{:}08{:}02{.}818 \dashrightarrow 00{:}08{:}04{.}888$ modifications are found on T RNA

NOTE Confidence: 0.6782445425

 $00{:}08{:}04.888 \dashrightarrow 00{:}08{:}07.068$ that is mitochondria encoded to RNA

NOTE Confidence: 0.6782445425

 $00{:}08{:}07{.}068 \dashrightarrow 00{:}08{:}08{.}873$ and those modifications are are.

 $00:08:08.880 \longrightarrow 00:08:11.184$ Important for translation at

NOTE Confidence: 0.6782445425

 $00{:}08{:}11{.}184 \dashrightarrow 00{:}08{:}14{.}270$ the above processes.

NOTE Confidence: 0.6782445425

 $00:08:14.270 \longrightarrow 00:08:16.634$ So I typically don't talk a

NOTE Confidence: 0.6782445425

 $00:08:16.634 \rightarrow 00:08:18.210$ whole lot about pathology,

NOTE Confidence: 0.6782445425

 $00{:}08{:}18{.}210 \dashrightarrow 00{:}08{:}21{.}059$ but I thought this crowd would be

NOTE Confidence: 0.6782445425

 $00:08{:}21.059 \dashrightarrow 00{:}08{:}24.400$ interested to know that a Baron or NOTE Confidence: 0.6782445425

00:08:24.400 --> 00:08:26.436 altered accumulation of tyranny

NOTE Confidence: 0.6782445425

 $00:08:26.436 \rightarrow 00:08:29.124$ modifications are are associated with

NOTE Confidence: 0.6782445425

 $00:08:29.124 \dashrightarrow 00:08:31.769$ a variety of pathological disease.

NOTE Confidence: 0.6782445425

00:08:31.770 --> 00:08:33.870 So we have mitochondrial disease

NOTE Confidence: 0.6782445425

 $00{:}08{:}33{.}870 \dashrightarrow 00{:}08{:}35{.}970$ that are associated with mutations

NOTE Confidence: 0.6782445425

 $00:08:36.039 \rightarrow 00:08:38.230$ on enzymes that are involved in the

NOTE Confidence: 0.6782445425

00:08:38.230 --> 00:08:40.387 synthesis of a T RNA modifications

NOTE Confidence: 0.6782445425

 $00{:}08{:}40{.}387 \dashrightarrow 00{:}08{:}42{.}297$ in the mitochondria you have

NOTE Confidence: 0.6782445425

 $00{:}08{:}42.297 \dashrightarrow 00{:}08{:}44.448$ disease that are affect.

NOTE Confidence: 0.6782445425

 $00:08:44.448 \longrightarrow 00:08:46.515$ Neurological defects associated

- NOTE Confidence: 0.6782445425
- 00:08:46.515 --> 00:08:49.960 with cancer and even diabetes.
- NOTE Confidence: 0.6782445425
- $00:08:49.960 \longrightarrow 00:08:52.738$ So the slide is really small.
- NOTE Confidence: 0.6782445425
- $00:08:52.740 \longrightarrow 00:08:54.508$ So the intention here is not for you
- NOTE Confidence: 0.6782445425
- $00:08:54.508 \rightarrow 00:08:56.556$ to read all the disease that are found,
- NOTE Confidence: 0.6782445425
- 00:08:56.560 --> 00:08:58.774 but you can read more about
- NOTE Confidence: 0.6782445425
- $00:08:58.774 \longrightarrow 00:09:00.810$ this in this Suzuki paper.
- NOTE Confidence: 0.6782445425
- 00:09:00.810 00:09:02.646 This is not my my literature,
- NOTE Confidence: 0.6782445425
- $00:09:02.650 \longrightarrow 00:09:04.876$ but it's a paper from a leading
- NOTE Confidence: 0.6782445425
- 00:09:04.876 --> 00:09:06.682 scientist on the ***** tyranny
- NOTE Confidence: 0.6782445425
- $00{:}09{:}06{.}682 \dashrightarrow 00{:}09{:}09{.}356$ modification field and you can get a
- NOTE Confidence: 0.6782445425
- $00:09:09.356 \rightarrow 00:09:12.627$ good idea of the variety of metabolic
- NOTE Confidence: 0.6782445425
- $00:09:12.627 \rightarrow 00:09:14.575$ consequences associated with this.
- NOTE Confidence: 0.6782445425
- 00:09:14.580 --> 00:09:18.300 Function of T RNA modifications.
- NOTE Confidence: 0.6782445425
- 00:09:18.300 --> 00:09:20.684 So in a recent review did on in
- NOTE Confidence: 0.6782445425
- $00:09:20.684 \rightarrow 00:09:22.870$ Dagley has stated that dysfunctional
- NOTE Confidence: 0.6782445425

 $00:09:22.870 \longrightarrow 00:09:25.390$ protein synthesis at the level

NOTE Confidence: 0.6782445425

 $00:09:25.390 \longrightarrow 00:09:27.260$ of translation elongation,

NOTE Confidence: 0.6782445425

 $00{:}09{:}27.260 \dashrightarrow 00{:}09{:}30.438$ so at point where T RNA modifications

NOTE Confidence: 0.6782445425

 $00{:}09{:}30{.}438 \dashrightarrow 00{:}09{:}33{.}108$ become relevant is now recognized as

NOTE Confidence: 0.6782445425

 $00:09:33.108 \longrightarrow 00:09:35.636$ a major pathophysiological driver in

NOTE Confidence: 0.6782445425

 $00:09:35.636 \rightarrow 00:09:38.496$ many human disease including cancer.

NOTE Confidence: 0.6782445425

 $00:09:38.500 \longrightarrow 00:09:41.594$ So this topic of research is really

NOTE Confidence: 0.6782445425

 $00:09:41.594 \dashrightarrow 00:09:43.845$ important and and oftentimes

NOTE Confidence: 0.6782445425

 $00{:}09{:}43.845 \dashrightarrow 00{:}09{:}46.350$ overlooked one understanding.

NOTE Confidence: 0.6782445425

 $00:09:46.350 \dashrightarrow 00:09:50.598$ A disease phenotype and molecular level.

NOTE Confidence: 0.6782445425

 $00{:}09{:}50.600 \dashrightarrow 00{:}09{:}52.598$ So the modification of interest that

NOTE Confidence: 0.6782445425

 $00:09:52.598 \dashrightarrow 00:09:55.477$ I want to share with you about is a

NOTE Confidence: 0.6782445425

 $00:09:55.477 \dashrightarrow 00:09:58.108$ modification that it's a 2 by your audience.

NOTE Confidence: 0.6782445425

 $00:09:58.110 \longrightarrow 00:09:59.710$ It's a modification that involves

NOTE Confidence: 0.6782445425

 $00:09:59.710 \longrightarrow 00:10:01.653$ sulfur and that you know that's

NOTE Confidence: 0.6782445425

 $00:10:01.653 \longrightarrow 00:10:03.620$ kind of it's fits into the whole

 $00:10:03.620 \rightarrow 00:10:05.324$ umbrella of my research program

NOTE Confidence: 0.6782445425

 $00{:}10{:}05{.}324 \dashrightarrow 00{:}10{:}07{.}478$ that we will understand how sulfur

NOTE Confidence: 0.6782445425

 $00:10:07.478 \rightarrow 00:10:09.283$ containing cofactors are assembled.

NOTE Confidence: 0.6782445425

 $00{:}10{:}09{.}283 \dashrightarrow 00{:}10{:}12{.}169$ So this modification is found at

NOTE Confidence: 0.6782445425

 $00:10:12.169 \rightarrow 00:10:14.858$ the wobble position of tyranny,

NOTE Confidence: 0.6782445425

 $00{:}10{:}14.860 \dashrightarrow 00{:}10{:}16.756$ so interacts with the last space

NOTE Confidence: 0.6782445425

 $00:10:16.756 \rightarrow 00:10:18.973$ on the codon and it's phylogenetic

NOTE Confidence: 0.6782445425

 $00:10:18.973 \longrightarrow 00:10:20.737$ conserved in all three.

NOTE Confidence: 0.6782445425

 $00{:}10{:}20.740 \dashrightarrow 00{:}10{:}22.876$ Domains of life and it's present

NOTE Confidence: 0.6782445425

 $00:10:22.876 \rightarrow 00:10:24.990$ in terminating codes for glutamine,

NOTE Confidence: 0.6782445425

 $00:10:24.990 \longrightarrow 00:10:26.547$ lysine and glutamate.

NOTE Confidence: 0.6782445425

 $00{:}10{:}26{.}547 \dashrightarrow 00{:}10{:}29{.}661$ And the importance of this modification

NOTE Confidence: 0.6782445425

 $00{:}10{:}29.661 \dashrightarrow 00{:}10{:}33.047$ is that introduction of a soul for a

NOTE Confidence: 0.6782445425

 $00{:}10{:}33.047 \dashrightarrow 00{:}10{:}35.869$ two position of uridine ring allows

NOTE Confidence: 0.6782445425

 $00{:}10{:}35{.}870 \dashrightarrow 00{:}10{:}38{.}455$ canonical base pair formation with

 $00:10:38.455 \rightarrow 00:10:42.350$ adenine for let's say AAA cordon of lysine.

NOTE Confidence: 0.6782445425

00:10:42.350 --> 00:10:44.625 But also taught totalization of

NOTE Confidence: 0.6782445425

 $00{:}10{:}44.625 \dashrightarrow 00{:}10{:}47.472$ this modification allows for non

NOTE Confidence: 0.6782445425

 $00:10:47.472 \rightarrow 00:10:49.784$ canonical base pair formations.

NOTE Confidence: 0.6782445425

 $00:10:49.790 \longrightarrow 00:10:51.710$ So in this case the you can base.

NOTE Confidence: 0.6782445425

 $00{:}10{:}51{.}710 \dashrightarrow 00{:}10{:}56{.}110$ Pair with the G so lack of those

NOTE Confidence: 0.6782445425

 $00{:}10{:}56.110 \dashrightarrow 00{:}10{:}59.096$ modifications that causes, you know,

NOTE Confidence: 0.6782445425

 $00:10:59.096 \rightarrow 00:11:00.620$ severe metabolic consequences.

NOTE Confidence: 0.6782445425

 $00{:}11{:}00{.}620 \dashrightarrow 00{:}11{:}03{.}436$ What it's what it's known that is inhuman.

NOTE Confidence: 0.6782445425

 $00{:}11{:}03{.}440 \dashrightarrow 00{:}11{:}06{.}415$ This modification is found both in the

NOTE Confidence: 0.6782445425

 $00{:}11{:}06{.}415 \dashrightarrow 00{:}11{:}10{.}190$ cytosolic T RNA is in the mitochondrial DNA.

NOTE Confidence: 0.6782445425

 $00:11:10.190 \rightarrow 00:11:10.790$ Interestingly,

NOTE Confidence: 0.6782445425

00:11:10.790 --> 00:11:13.790 the biosynthetic pathway to modify

NOTE Confidence: 0.6782445425

 $00:11:13.790 \rightarrow 00:11:16.469$ terminating the cytosol is different

NOTE Confidence: 0.6782445425

 $00:11:16.469 \rightarrow 00:11:19.669$ than the one that is used to synthesize

NOTE Confidence: 0.78447247952

 $00:11:19.748 \longrightarrow 00:11:22.208 2$ thymidine in the mitochondria.

00:11:22.210 --> 00:11:24.316 And the mitochondria pathway is similar

NOTE Confidence: 0.78447247952

 $00{:}11{:}24{.}316 \dashrightarrow 00{:}11{:}27{.}167$ to that of what it's found in bacteria

NOTE Confidence: 0.78447247952

 $00:11:27.167 \rightarrow 00:11:29.620$ so reinforces the idea that you know,

NOTE Confidence: 0.78447247952

00:11:29.620 --> 00:11:32.000 bacteria was a ancient microorganisms

NOTE Confidence: 0.78447247952

 $00:11:32.000 \rightarrow 00:11:35.855$ that had been gold to into ****** cells.

NOTE Confidence: 0.78447247952

00:11:35.855 --> 00:11:38.885 So here's some good examples of

NOTE Confidence: 0.78447247952

 $00:11:38.885 \rightarrow 00:11:41.264$ biosynthetic enzymes involved in the

NOTE Confidence: 0.78447247952

 $00:11:41.264 \rightarrow 00:11:43.622$ cities of two pyridine and mutations

NOTE Confidence: 0.78447247952

00:11:43.622 -> 00:11:46.239 have been found in those genes

NOTE Confidence: 0.78447247952

 $00:11:46.239 \rightarrow 00:11:48.424$ and they are diseased phenotype.

NOTE Confidence: 0.78447247952

00:11:48.430 --> 00:11:49.798 So I'm not really.

NOTE Confidence: 0.5854362895

 $00{:}11{:}52{.}170 \dashrightarrow 00{:}11{:}55{.}026$ A sanitise that studies human disease,

NOTE Confidence: 0.5854362895

 $00:11:55.030 \rightarrow 00:11:57.478$ but that's my effort to to connect with

NOTE Confidence: 0.5854362895

 $00{:}11{:}57{.}478 \dashrightarrow 00{:}12{:}00{.}266$ the audience by primary interest is really

NOTE Confidence: 0.5854362895

 $00:12:00.266 \rightarrow 00:12:02.381$ trying to understand bacterial metabolism.

 $00{:}12{:}02{.}390 \dashrightarrow 00{:}12{:}05{.}030$ And what we know is that in bacteria

NOTE Confidence: 0.5854362895

 $00{:}12{:}05{.}030 \dashrightarrow 00{:}12{:}08{.}597$ lack of two pyridine or mutations in the

NOTE Confidence: 0.5854362895

 $00{:}12{:}08.597 \dashrightarrow 00{:}12{:}11.037$ the biosynthetic components of tooth

NOTE Confidence: 0.5854362895

 $00:12:11.037 \rightarrow 00:12:13.397$ iodine leads to compromise cellular

NOTE Confidence: 0.5854362895

 $00:12:13.397 \rightarrow 00:12:16.682$ viability and in some cases including the

NOTE Confidence: 0.5854362895

 $00{:}12{:}16.682 \dashrightarrow 00{:}12{:}19.466$ organisms that I am interested about,

NOTE Confidence: 0.5854362895

 $00:12:19.470 \longrightarrow 00:12:21.430$ this pathway is fully essential

NOTE Confidence: 0.5854362895

 $00:12:21.430 \longrightarrow 00:12:22.991$ for the organization. Survive.

NOTE Confidence: 0.5854362895

 $00{:}12{:}22{.}991 \dashrightarrow 00{:}12{:}25{.}277$ OK, so it's it's an essential

NOTE Confidence: 0.5854362895

00:12:25.277 --> 00:12:26.039 cellular process,

NOTE Confidence: 0.5854362895

 $00{:}12{:}26.040 \dashrightarrow 00{:}12{:}29.386$ which makes very interesting if you think

NOTE Confidence: 0.5854362895

 $00:12:29.386 \longrightarrow 00:12:31.898$ about pathogenic bacteria and how you

NOTE Confidence: 0.5854362895

 $00{:}12{:}31.898 \dashrightarrow 00{:}12{:}37.418$ can discover new metabolic interventions for.

NOTE Confidence: 0.5854362895

 $00{:}12{:}37{.}420 \dashrightarrow 00{:}12{:}39{.}800$ For the treatment of infections

NOTE Confidence: 0.5854362895

 $00:12:39.800 \longrightarrow 00:12:42.803$ caused by pathogenic so in the

NOTE Confidence: 0.5854362895

 $00:12:42.803 \rightarrow 00:12:44.967$ synthesis of new antibiotics.

- NOTE Confidence: 0.5854362895
- $00:12:44.970 \longrightarrow 00:12:47.772$ So that's the story that I
- NOTE Confidence: 0.5854362895
- $00:12:47.772 \longrightarrow 00:12:50.789$ wanted to tell you about how?
- NOTE Confidence: 0.5854362895
- $00{:}12{:}50.790 \dashrightarrow 00{:}12{:}53.966$ My students and I went on this mission
- NOTE Confidence: 0.5854362895
- 00:12:53.966 --> 00:12:56.738 to really understand and identify
- NOTE Confidence: 0.5854362895
- $00{:}12{:}56.738 \dashrightarrow 00{:}12{:}59.408$ the biosynthetic components of two
- NOTE Confidence: 0.5854362895
- 00:12:59.408 --> 00:13:01.790 pyridine and Bacillus subtilis,
- NOTE Confidence: 0.5854362895
- $00{:}13{:}01{.}790 \dashrightarrow 00{:}13{:}04{.}409$ and in the work that we have done more
- NOTE Confidence: 0.5854362895
- $00:13:04.409 \rightarrow 00:13:06.380$ recently to uncover the additional
- NOTE Confidence: 0.5854362895
- $00{:}13{:}06{.}380 \dashrightarrow 00{:}13{:}07{.}992$ functions that this modification
- NOTE Confidence: 0.5854362895
- $00:13:07.992 \rightarrow 00:13:10.262$ may be playing a role in,
- NOTE Confidence: 0.5854362895
- $00{:}13{:}10.262 \dashrightarrow 00{:}13{:}12.390$ in this particular Organism.
- NOTE Confidence: 0.5854362895
- $00:13:12.390 \longrightarrow 00:13:14.945$ So that's the work of two very
- NOTE Confidence: 0.5854362895
- $00{:}13{:}14.945 \dashrightarrow 00{:}13{:}16.748$ talented graduate students in my lab,
- NOTE Confidence: 0.5854362895
- 00:13:16.750 --> 00:13:18.112 I, Catherine Black,
- NOTE Confidence: 0.5854362895
- 00:13:18.112 --> 00:13:20.836 and actually Edwards actually has graduated.
- NOTE Confidence: 0.5854362895

- $00:13:20.840 \longrightarrow 00:13:22.076$ Uh, last month.
- NOTE Confidence: 0.5854362895
- 00:13:22.076 --> 00:13:24.520 So she she's now off to do bigger
- NOTE Confidence: 0.5854362895
- $00:13:24.520 \longrightarrow 00:13:26.180$ and better things in her life,
- NOTE Confidence: 0.5854362895
- $00{:}13{:}26.180 \dashrightarrow 00{:}13{:}28.052$ but I'm grateful for the discoveries
- NOTE Confidence: 0.5854362895
- $00{:}13{:}28.052 \dashrightarrow 00{:}13{:}29.300$ that she made here.
- NOTE Confidence: 0.5854362895
- $00:13:29.300 \longrightarrow 00:13:31.112$ So there are three main points
- NOTE Confidence: 0.5854362895
- $00{:}13{:}31{.}112 \dashrightarrow 00{:}13{:}34{.}003$ that I want to convey here on our
- NOTE Confidence: 0.5854362895
- $00:13:34.003 \rightarrow 00:13:36.018$ study of two pyridine biosynthesis.
- NOTE Confidence: 0.5854362895
- 00:13:36.020 --> 00:13:38.340 It's our experimental approach
- NOTE Confidence: 0.5854362895
- $00:13:38.340 \rightarrow 00:13:40.660$ to identify biosynthetic enzymes,
- NOTE Confidence: 0.5854362895
- $00:13:40.660 \longrightarrow 00:13:42.280$ the function of two,
- NOTE Confidence: 0.5854362895
- $00:13:42.280 \rightarrow 00:13:45.356$ two pyridine as a marker or potentially
- NOTE Confidence: 0.5854362895
- $00:13:45.356 \longrightarrow 00:13:48.698$ sensor of so far availability in
- NOTE Confidence: 0.5854362895
- $00:13:48.698 \longrightarrow 00:13:51.049$ Bacillus subtilis and how we.
- NOTE Confidence: 0.5854362895
- $00:13:51.050 \rightarrow 00:13:53.406$ Understand the biochemical principles
- NOTE Confidence: 0.5854362895
- $00:13:53.406 \rightarrow 00:13:56.940$ by which those enzymes operate that

- NOTE Confidence: 0.5854362895
- $00:13:57.026 \longrightarrow 00:13:59.581$ restrict and direct their roles

 $00{:}13{:}59{.}581 \dashrightarrow 00{:}14{:}01{.}625$ in the sulfur metabolism.

NOTE Confidence: 0.703341018333333

 $00{:}14{:}04{.}510 \dashrightarrow 00{:}14{:}06{.}406$ Before I dive in as that,

NOTE Confidence: 0.703341018333333

 $00:14:06.410 \longrightarrow 00:14:08.849$ I wanted to kind of like show you some

NOTE Confidence: 0.703341018333333

 $00:14:08.849 \rightarrow 00:14:11.764$ key points so you can have an appreciation

NOTE Confidence: 0.703341018333333

 $00{:}14{:}11.764 \dashrightarrow 00{:}14{:}14.301$ for the complexity of studying those

NOTE Confidence: 0.703341018333333

00:14:14.301 -> 00:14:16.686 systems at the biochemical level.

NOTE Confidence: 0.703341018333333

 $00{:}14{:}16.690 \dashrightarrow 00{:}14{:}19.840$ So what we know is that in the centers of

NOTE Confidence: 0.703341018333333

 $00{:}14{:}19{.}926 \dashrightarrow 00{:}14{:}22{.}926$ Tyler cofactors and I mentioned before,

NOTE Confidence: 0.703341018333333

 $00{:}14{:}22{.}930 \dashrightarrow 00{:}14{:}25{.}714$ I'm interested in the cities of all the

NOTE Confidence: 0.703341018333333

 $00:14:25.714 \rightarrow 00:14:27.568$ biomolecules showing here on this slide.

NOTE Confidence: 0.703341018333333

 $00{:}14{:}27{.}570 \dashrightarrow 00{:}14{:}29{.}818$ What we know is that the first staff

NOTE Confidence: 0.703341018333333

00:14:29.818 --> 00:14:32.277 on super mobilization is catalyzed by

NOTE Confidence: 0.703341018333333

 $00{:}14{:}32.277 \dashrightarrow 00{:}14{:}34.567$ an enzyme called cysteine disulphide.

NOTE Confidence: 0.703341018333333

 $00:14:34.570 \longrightarrow 00:14:38.050$ So those enzymes they they use a ping NOTE Confidence: 0.703341018333333

 $00:14:38.050 \longrightarrow 00:14:40.847$ pong mechanism to bind sustain and

NOTE Confidence: 0.703341018333333

 $00:14:40.847 \rightarrow 00:14:43.607$ convert sustain into alanine and by

NOTE Confidence: 0.703341018333333

 $00:14:43.694 \rightarrow 00:14:47.733$ doing so they form a covalent sulfur

NOTE Confidence: 0.703341018333333

 $00{:}14{:}47.733 \dashrightarrow 00{:}14{:}49.464$ personified enzyme intermediate.

NOTE Confidence: 0.703341018333333

 $00{:}14{:}49{.}470 \dashrightarrow 00{:}14{:}52{.}398$ The sulfur then is transferred to

NOTE Confidence: 0.703341018333333

 $00{:}14{:}52{.}398 \dashrightarrow 00{:}14{:}54{.}823$ downstream pathway components involved in

NOTE Confidence: 0.703341018333333

 $00{:}14{:}54{.}823 \dashrightarrow 00{:}14{:}57{.}205$ the synthesis of iron sulfur clusters,

NOTE Confidence: 0.703341018333333

 $00{:}14{:}57{.}210 \dashrightarrow 00{:}15{:}01{.}430$ tail nucleosides or different vitamins.

NOTE Confidence: 0.703341018333333

 $00:15:01.430 \longrightarrow 00:15:04.820$ As in the case of tyramine, lipoic acid,

NOTE Confidence: 0.703341018333333

 $00:15:04.820 \longrightarrow 00:15:07.850$ biotin, so on and so forth.

NOTE Confidence: 0.703341018333333

 $00{:}15{:}07{.}850 \dashrightarrow 00{:}15{:}11{.}126$ But it's a complicated here is that

NOTE Confidence: 0.703341018333333

00:15:11.130 --> 00:15:13.286 if you have at least in humans,

NOTE Confidence: 0.703341018333333

00:15:13.290 --> 00:15:14.890 you have one single enzyme,

NOTE Confidence: 0.703341018333333

 $00{:}15{:}14.890 \dashrightarrow 00{:}15{:}17.235$ NFS one that is responsible for the

NOTE Confidence: 0.703341018333333

 $00{:}15{:}17.235 \dashrightarrow 00{:}15{:}19.340$ synthesis of all time nucleosides

NOTE Confidence: 0.703341018333333

 $00:15:19.340 \longrightarrow 00:15:20.560$ in the human genome.

 $00:15:20.560 \longrightarrow 00:15:22.390$ So that's that enzyme is found

NOTE Confidence: 0.703341018333333

 $00{:}15{:}22{.}453 \dashrightarrow 00{:}15{:}23{.}650$ in the mitochondria.

NOTE Confidence: 0.703341018333333

00:15:23.650 --> 00:15:26.810 In some study model systems like E coli,

NOTE Confidence: 0.703341018333333

 $00{:}15{:}26{.}810 \dashrightarrow 00{:}15{:}30{.}642$ you also have a primary enzyme and then

NOTE Confidence: 0.703341018333333

 $00:15:30.642 \rightarrow 00:15:34.302$ the sulfur transfer pathway here is

NOTE Confidence: 0.703341018333333

 $00:15:34.302 \rightarrow 00:15:36.946$ shared across different pathways, right?

NOTE Confidence: 0.703341018333333

 $00:15:36.946 \longrightarrow 00:15:38.050$ So you have one.

NOTE Confidence: 0.703341018333333

 $00:15:38.050 \rightarrow 00:15:40.210$ Primary sulfur donor then and then

NOTE Confidence: 0.703341018333333

 $00{:}15{:}40{.}210 \dashrightarrow 00{:}15{:}42{.}612$ that sulfur is traffic to different

NOTE Confidence: 0.703341018333333

 $00:15:42.612 \longrightarrow 00:15:44.852$ pathway intermediates and in some

NOTE Confidence: 0.703341018333333

 $00:15:44.852 \rightarrow 00:15:46.589$ cases those biosynthetic intermediates

NOTE Confidence: 0.703341018333333

 $00{:}15{:}46{.}589 \dashrightarrow 00{:}15{:}49{.}487$ are shared as in the case of two five

NOTE Confidence: 0.703341018333333

 $00{:}15{:}49{.}490 \dashrightarrow 00{:}15{:}52{.}964$ year adine and moco Biogenesis which

NOTE Confidence: 0.703341018333333

 $00{:}15{:}52{.}964 \dashrightarrow 00{:}15{:}56{.}889$ is also a protein called factor.

NOTE Confidence: 0.703341018333333

 $00{:}15{:}56{.}890 \dashrightarrow 00{:}15{:}59{.}368$ To complicate things a little bit more,

 $00:15:59.370 \longrightarrow 00:16:02.798$ is that one interest that I had for

NOTE Confidence: 0.703341018333333

 $00:16:02.798 \rightarrow 00:16:04.770$ many years and I guess that's where

NOTE Confidence: 0.703341018333333

00:16:04.770 --> 00:16:06.684 most of my publications come from,

NOTE Confidence: 0.703341018333333

 $00:16:06.690 \rightarrow 00:16:08.646$ is really trying to understand the

NOTE Confidence: 0.703341018333333

 $00:16:08.646 \rightarrow 00:16:10.752$ pathway that leads to the synthesis

NOTE Confidence: 0.703341018333333

00:16:10.752 --> 00:16:12.228 of iron sulfur clusters,

NOTE Confidence: 0.703341018333333

 $00:16:12.230 \rightarrow 00:16:13.818$ very essential protein cofactors.

NOTE Confidence: 0.703341018333333

 $00:16:13.818 \rightarrow 00:16:17.339$ And then what we want to do is like

NOTE Confidence: 0.703341018333333

 $00:16:17.339 \rightarrow 00:16:19.475$ when we try to deconvolute those

NOTE Confidence: 0.703341018333333

00:16:19.475 --> 00:16:21.733 pathways and try to understand

NOTE Confidence: 0.703341018333333

 $00{:}16{:}21.733 \dashrightarrow 00{:}16{:}23.565$ metabolic defects associated with

NOTE Confidence: 0.703341018333333

 $00:16:23.565 \rightarrow 00:16:26.002$ the initial sulfur mobilization step.

NOTE Confidence: 0.703341018333333

 $00:16:26.002 \rightarrow 00:16:29.530$ It's quite complex because what we see

NOTE Confidence: 0.703341018333333

 $00:16:29.610 \rightarrow 00:16:32.754$ is that there are so iron sulfur enzyme,

NOTE Confidence: 0.703341018333333

 $00:16:32.760 \longrightarrow 00:16:35.202$ so enzymes that depend on iron

NOTE Confidence: 0.703341018333333

 $00:16:35.202 \rightarrow 00:16:37.837$ sulfur cluster for the synthesis of

 $00:16:37.837 \rightarrow 00:16:40.115$ other sulfur containing metabolites.

NOTE Confidence: 0.703341018333333

 $00{:}16{:}40.115 \dashrightarrow 00{:}16{:}45.033$ So when you disrupt the initial steps on

NOTE Confidence: 0.703341018333333

 $00{:}16{:}45.033 \dashrightarrow 00{:}16{:}47.998$ sulphur mobilization so for instance.

NOTE Confidence: 0.703341018333333

 $00:16:48.000 \rightarrow 00:16:50.090$ For the synthesis of tyramine,

NOTE Confidence: 0.703341018333333

00:16:50.090 --> 00:16:52.268 you don't really know if you're

NOTE Confidence: 0.703341018333333

 $00{:}16{:}52{.}268 \dashrightarrow 00{:}16{:}54{.}593$ disrupting the primary route for sulfur

NOTE Confidence: 0.703341018333333

 $00:16:54.593 \rightarrow 00:16:57.023$ transfer or if you're inactivating a

NOTE Confidence: 0.703341018333333

 $00:16:57.023 \rightarrow 00:16:58.989$ biosynthetic enzyme that requires an

NOTE Confidence: 0.703341018333333

00:16:58.989 --> 00:17:01.167 iron sulfur cluster for its activity.

NOTE Confidence: 0.703341018333333

 $00{:}17{:}01{.}170 \dashrightarrow 00{:}17{:}03.966$ So you have this intertwined metabolic

NOTE Confidence: 0.703341018333333

 $00:17:03.966 \longrightarrow 00:17:06.397$ pathways that you have dependency

NOTE Confidence: 0.703341018333333

 $00{:}17{:}06{.}397 \dashrightarrow 00{:}17{:}09{.}331$ of a super containing cofactor in

NOTE Confidence: 0.703341018333333

 $00{:}17{:}09{.}331 \dashrightarrow 00{:}17{:}12{.}533$ the biosynthesis of another super

NOTE Confidence: 0.703341018333333

00:17:12.533 --> 00:17:16.486 containing cofactor. OK.

NOTE Confidence: 0.703341018333333

 $00{:}17{:}16.486 \dashrightarrow 00{:}17{:}23.310$ So one primary metabolic.

 $00:17:23.310 \longrightarrow 00:17:25.725$ A component that we look at it's

NOTE Confidence: 0.703341018333333

 $00{:}17{:}25.725 \dashrightarrow 00{:}17{:}28.127$ tyranny and how T RNA is modified.

NOTE Confidence: 0.703341018333333

 $00:17:28.130 \longrightarrow 00:17:31.154$ And this is really great because

NOTE Confidence: 0.703341018333333

 $00{:}17{:}31{.}154 \dashrightarrow 00{:}17{:}35{.}187$ on T RNA modification of a pool you

NOTE Confidence: 0.703341018333333

 $00:17:35.187 \longrightarrow 00:17:36.627$ can identify pathways,

NOTE Confidence: 0.703341018333333

 $00:17:36.630 \rightarrow 00:17:38.474$ enzymes that contain iron,

NOTE Confidence: 0.703341018333333

 $00{:}17{:}38{.}474 \dashrightarrow 00{:}17{:}41{.}240$ sulfur clusters and then they would.

NOTE Confidence: 0.64577314875

00:17:43.700 --> 00:17:46.228 Transfer sulfur to the

NOTE Confidence: 0.64577314875

 $00{:}17{:}46.228 \dashrightarrow 00{:}17{:}48.756$ cities of this cofactor.

NOTE Confidence: 0.64577314875

 $00:17:48.760 \longrightarrow 00:17:50.116$ So this is an example here.

NOTE Confidence: 0.64577314875

 $00{:}17{:}50{.}120 \dashrightarrow 00{:}17{:}53{.}325$ The mutations that deplete this

NOTE Confidence: 0.64577314875

00:17:53.325 --> 00:17:55.248 modification causes diabetes,

NOTE Confidence: 0.64577314875

 $00:17:55.250 \longrightarrow 00:17:58.029$ for instance, so and the enzyme that

NOTE Confidence: 0.64577314875

 $00{:}17{:}58.029 \dashrightarrow 00{:}18{:}01.114$ does that is an enzyme that contains

NOTE Confidence: 0.64577314875

 $00:18:01.114 \rightarrow 00:18:03.832$ an iron sulfur cluster you have.

NOTE Confidence: 0.64577314875

 $00:18:03.840 \longrightarrow 00:18:07.070$ Sometimes I miss the mouse.

 $00{:}18{:}07{.}070 \dashrightarrow 00{:}18{:}09{.}200$ You have pathways like the S2

NOTE Confidence: 0.64577314875

 $00:18:09.200 \longrightarrow 00:18:11.508$ you pathway that do not require

NOTE Confidence: 0.64577314875

00:18:11.508 --> 00:18:13.944 iron super enzymes and then you

NOTE Confidence: 0.64577314875

00:18:13.944 --> 00:18:16.221 have empathy is not shown here

NOTE Confidence: 0.64577314875

00:18:16.221 --> 00:18:18.620 that do not contain sulfur but it

NOTE Confidence: 0.64577314875

 $00{:}18{:}18{.}620 \dashrightarrow 00{:}18{:}20{.}170$ depends on iron sulfur cluster.

NOTE Confidence: 0.64577314875

 $00{:}18{:}20{.}170 \dashrightarrow 00{:}18{:}22{.}978$ So you can interrogate the cells

NOTE Confidence: 0.64577314875

 $00{:}18{:}22.978 \dashrightarrow 00{:}18{:}24.850$ under different conditions and

NOTE Confidence: 0.64577314875

 $00:18:24.934 \longrightarrow 00:18:27.388$ you can extract the that tyranny.

NOTE Confidence: 0.64577314875

 $00:18:27.390 \longrightarrow 00:18:29.406$ And the primary tool that we use

NOTE Confidence: 0.64577314875

 $00:18:29.406 \longrightarrow 00:18:31.948$ here is to purify those two RNA

NOTE Confidence: 0.64577314875

00:18:31.948 --> 00:18:34.360 molecules and then analyze the relative

NOTE Confidence: 0.64577314875

 $00{:}18{:}34{.}431 \dashrightarrow 00{:}18{:}37{.}179$ abundance of all those nucleosides using.

NOTE Confidence: 0.64577314875

00:18:37.180 --> 00:18:38.624 High resolution mass spectrometry.

NOTE Confidence: 0.64577314875

 $00:18:38.624 \longrightarrow 00:18:40.429$ So when we do that,

 $00:18:40.430 \rightarrow 00:18:43.174$ we not only analyze the analyte of interest

NOTE Confidence: 0.64577314875

 $00{:}18{:}43{.}174 \dashrightarrow 00{:}18{:}46{.}108$ as as to you in this particular case,

NOTE Confidence: 0.64577314875

 $00{:}18{:}46{.}110 \dashrightarrow 00{:}18{:}48{.}302$ but we look at the relative levels of

NOTE Confidence: 0.64577314875

 $00{:}18{:}48{.}302 \dashrightarrow 00{:}18{:}50{.}310$ all those different modifications.

NOTE Confidence: 0.64577314875

 $00{:}18{:}50{.}310 \dashrightarrow 00{:}18{:}52{.}230$ This is important because for

NOTE Confidence: 0.64577314875

 $00{:}18{:}52{.}230 \dashrightarrow 00{:}18{:}55{.}003$ instance in the case of two tire

NOTE Confidence: 0.64577314875

 $00:18:55.003 \rightarrow 00:18:57.987$ reading that is in this box here this

NOTE Confidence: 0.64577314875

 $00{:}18{:}57{.}987 \dashrightarrow 00{:}19{:}00{.}154$ modification comes along with additional

NOTE Confidence: 0.64577314875

 $00{:}19{:}00{.}154 \dashrightarrow 00{:}19{:}02.609$ modifications on the uridine base.

NOTE Confidence: 0.64577314875

 $00{:}19{:}02.610 \dashrightarrow 00{:}19{:}04.986$ So if we really want to quantify the effects

NOTE Confidence: 0.64577314875

 $00:19:04.986 \longrightarrow 00:19:07.219$ on the biosynthesis of two thymidine.

NOTE Confidence: 0.64577314875

 $00{:}19{:}07{.}220 \dashrightarrow 00{:}19{:}09{.}890$ We have to quantify all those

NOTE Confidence: 0.64577314875

 $00{:}19{:}09{.}890 \dashrightarrow 00{:}19{:}11{.}670$ different metabolites and understand

NOTE Confidence: 0.64577314875

 $00{:}19{:}11.741 \dashrightarrow 00{:}19{:}13.897$ the their relative accumulation.

NOTE Confidence: 0.819992196923077

 $00:19:16.270 \dashrightarrow 00:19:18.754$ Umm. Another point to consider when

NOTE Confidence: 0.819992196923077

 $00{:}19{:}18.754 \dashrightarrow 00{:}19{:}21.569$ pursuing this analysis is that the levels,

- NOTE Confidence: 0.819992196923077
- $00:19:21.570 \longrightarrow 00:19:23.270$ the relative levels of tyranny,
- NOTE Confidence: 0.819992196923077
- $00{:}19{:}23.270 \dashrightarrow 00{:}19{:}28.688$ modifications, they vary with growth phase,
- NOTE Confidence: 0.819992196923077
- $00:19:28.690 \longrightarrow 00:19:29.644$ growth conditions,
- NOTE Confidence: 0.819992196923077
- $00:19:29.644 \rightarrow 00:19:32.983$ temperatures and so on and so forth.
- NOTE Confidence: 0.819992196923077
- $00{:}19{:}32{.}990 \dashrightarrow 00{:}19{:}35{.}702$ So the notion that TNA is modified and
- NOTE Confidence: 0.819992196923077
- $00{:}19{:}35{.}702 \dashrightarrow 00{:}19{:}39{.}091$ now is fully functional to perform roles
- NOTE Confidence: 0.819992196923077
- $00:19:39.091 \rightarrow 00:19:41.726$ in translation is really misleading.
- NOTE Confidence: 0.819992196923077
- $00:19:41.730 \longrightarrow 00:19:44.285$ What we know is that there are
- NOTE Confidence: 0.819992196923077
- $00:19:44.285 \longrightarrow 00:19:45.925$ degrees of modification that
- NOTE Confidence: 0.819992196923077
- $00:19:45.925 \longrightarrow 00:19:47.817$ confined to the functionality.
- NOTE Confidence: 0.819992196923077
- $00:19:47.820 \rightarrow 00:19:50.412$ Of that tyranny and therefore fine
- NOTE Confidence: 0.819992196923077
- $00:19:50.412 \longrightarrow 00:19:53.130$ tune the efficiency of translation.
- NOTE Confidence: 0.819992196923077
- $00:19:53.130 \longrightarrow 00:19:54.636$ So for instance,
- NOTE Confidence: 0.819992196923077
- $00{:}19{:}54.636 \dashrightarrow 00{:}19{:}57.648$ if you grow cells and the
- NOTE Confidence: 0.819992196923077
- $00:19:57.648 \rightarrow 00:19:58.662$ different temperatures,
- NOTE Confidence: 0.819992196923077

 $00:19:58.662 \rightarrow 00:20:01.734$ you can have a different loading

NOTE Confidence: 0.819992196923077

 $00:20:01.734 \longrightarrow 00:20:04.343$ of of modification and that's

NOTE Confidence: 0.819992196923077

 $00:20:04.343 \longrightarrow 00:20:06.438$ interpreted as improving the

NOTE Confidence: 0.819992196923077

 $00:20:06.438 \rightarrow 00:20:09.208$ rigidity of that anticodon loop.

NOTE Confidence: 0.819992196923077

 $00{:}20{:}09{.}210 \dashrightarrow 00{:}20{:}11.718$ So you can favor base pairing

NOTE Confidence: 0.819992196923077

 $00:20:11.718 \rightarrow 00:20:14.290$ information even in a higher temperature

NOTE Confidence: 0.819992196923077

 $00:20:14.290 \longrightarrow 00:20:18.870$ as in the case of the MSU I6A.

NOTE Confidence: 0.819992196923077

00:20:18.870 --> 00:20:21.330 You can also see a differential

NOTE Confidence: 0.819992196923077

 $00{:}20{:}21{.}330 \dashrightarrow 00{:}20{:}22{.}970$ accumulation of some modifications

NOTE Confidence: 0.819992196923077

 $00{:}20{:}23.040 \dashrightarrow 00{:}20{:}25.314$ under oxidative stress and this is

NOTE Confidence: 0.819992196923077

 $00{:}20{:}25{.}314 \dashrightarrow 00{:}20{:}27{.}317$ attributed because some of those

NOTE Confidence: 0.819992196923077

 $00:20:27.317 \rightarrow 00:20:28.985$ modifications they are dependent

NOTE Confidence: 0.819992196923077

00:20:28.985 --> 00:20:31.070 on enzymes that contain iron

NOTE Confidence: 0.819992196923077

 $00:20:31.070 \longrightarrow 00:20:33.610$ superclusters and then those clusters

NOTE Confidence: 0.819992196923077

 $00:20:33.610 \rightarrow 00:20:36.150$ are susceptible to oxidative damage.

NOTE Confidence: 0.819992196923077

 $00:20:36.150 \longrightarrow 00:20:38.142$ So you can have a different

 $00{:}20{:}38.142 \dashrightarrow 00{:}20{:}40.738$ accumulation as a sa readout for

NOTE Confidence: 0.819992196923077

 $00{:}20{:}40.738 \dashrightarrow 00{:}20{:}42.728$ oxidative stress in those cells.

NOTE Confidence: 0.809869931071428

00:20:45.740 --> 00:20:48.197 So, so when it's studying or trying

NOTE Confidence: 0.809869931071428

 $00:20:48.197 \rightarrow 00:20:51.180$ to assign a different pathways in the

NOTE Confidence: 0.809869931071428

 $00:20:51.180 \rightarrow 00:20:54.457$ organisms that have not been studied before

NOTE Confidence: 0.809869931071428

00:20:54.457 - 00:20:57.397 the the standard procedure to do that,

NOTE Confidence: 0.809869931071428

 $00:20:57.400 \longrightarrow 00:20:59.521$ it's like you take a pathway that

NOTE Confidence: 0.809869931071428

 $00{:}20{:}59{.}521 \dashrightarrow 00{:}21{:}01{.}464$ is well studied and established and

NOTE Confidence: 0.809869931071428

 $00{:}21{:}01{.}464 \dashrightarrow 00{:}21{:}03{.}718$ then you start to blast for that

NOTE Confidence: 0.809869931071428

 $00:21:03.781 \rightarrow 00:21:06.043$ gene in that particular Organism and

NOTE Confidence: 0.809869931071428

 $00:21:06.043 \rightarrow 00:21:07.881$ then you find equivalent components

NOTE Confidence: 0.809869931071428

 $00:21:07.881 \longrightarrow 00:21:10.128$ that you can make a good assumption

NOTE Confidence: 0.809869931071428

 $00{:}21{:}10{.}128 \dashrightarrow 00{:}21{:}12{.}252$ based on sequence analysis. So.

NOTE Confidence: 0.809869931071428

 $00{:}21{:}12{.}252 \dashrightarrow 00{:}21{:}15{.}148$ So when we start that that research that's.

NOTE Confidence: 0.809869931071428

 $00{:}21{:}15{.}150 \dashrightarrow 00{:}21{:}18.669$ Out of the office workflow to fish out those

00:21:18.669 --> 00:21:22.120 genes and and to do biochemical experiments.

NOTE Confidence: 0.809869931071428

 $00:21:22.120 \longrightarrow 00:21:25.060$ So but that's not really the case.

NOTE Confidence: 0.809869931071428

 $00:21:25.060 \rightarrow 00:21:27.328$ So when we compare the pathway found

NOTE Confidence: 0.809869931071428

 $00:21:27.328 \rightarrow 00:21:30.362$ in E coli that is where we study and

NOTE Confidence: 0.809869931071428

 $00:21:30.362 \rightarrow 00:21:32.660$ then we're trying to find equivalent

NOTE Confidence: 0.809869931071428

 $00:21:32.660 \dashrightarrow 00:21:35.354$ genes in the basal subtilis genome.

NOTE Confidence: 0.809869931071428

00:21:35.360 --> 00:21:37.782 We do not find a complete pathway

NOTE Confidence: 0.809869931071428

 $00{:}21{:}37.782 \dashrightarrow 00{:}21{:}40.984$ in terms of all the enzymes are not

NOTE Confidence: 0.809869931071428

 $00:21:40.984 \rightarrow 00:21:43.681$ really present in some enzymes are

NOTE Confidence: 0.809869931071428

 $00:21:43.681 \rightarrow 00:21:45.298$ missing suggesting that.

NOTE Confidence: 0.809869931071428

00:21:45.300 --> 00:21:48.912 Now you have perhaps an alternate mechanism

NOTE Confidence: 0.809869931071428

 $00:21:48.912 \rightarrow 00:21:51.719$ to synthesize that same cofactor.

NOTE Confidence: 0.809869931071428

 $00:21:51.720 \rightarrow 00:21:54.424$ And that's the case here for two pyridine.

NOTE Confidence: 0.809869931071428

 $00{:}21{:}54{.}430 \dashrightarrow 00{:}21{:}57{.}888$ So our attempts to search for all

NOTE Confidence: 0.809869931071428

 $00:21:57.888 \rightarrow 00:22:00.910$ those enzymes here showing red fail.

NOTE Confidence: 0.809869931071428

 $00:22:00.910 \rightarrow 00:22:03.310$ So that means that imbecile subtilis,

 $00{:}22{:}03{.}310 \dashrightarrow 00{:}22{:}05{.}865$ you don't have those pathways like 5

NOTE Confidence: 0.809869931071428

00:22:05.865 --> 00:22:08.210 pathway components are completely missing.

NOTE Confidence: 0.809869931071428

00:22:08.210 --> 00:22:09.462 So how you go,

NOTE Confidence: 0.809869931071428

00:22:09.462 --> 00:22:11.340 how you go from the Sistine,

NOTE Confidence: 0.809869931071428

 $00:22:11.340 \longrightarrow 00:22:13.392$ the sulfur race to the final

NOTE Confidence: 0.809869931071428

 $00:22:13.392 \longrightarrow 00:22:15.674$ enzyme in the pathway was the

NOTE Confidence: 0.809869931071428

 $00:22:15.674 \rightarrow 00:22:17.774$ question for that particular study.

NOTE Confidence: 0.809869931071428

 $00:22:17.780 \longrightarrow 00:22:21.540$ OK, So what we know is that in the collide.

NOTE Confidence: 0.809869931071428

 $00{:}22{:}21{.}540 \dashrightarrow 00{:}22{:}23{.}838$ Those pathways are really well studied.

NOTE Confidence: 0.809869931071428

00:22:23.840 --> 00:22:25.736 There's one primary enzyme,

NOTE Confidence: 0.809869931071428

 $00:22:25.736 \rightarrow 00:22:28.106$ there's three dominant sulfur receptors,

NOTE Confidence: 0.809869931071428

 $00{:}22{:}28.110 \dashrightarrow 00{:}22{:}29.640$ and then sulfur receptors showing

NOTE Confidence: 0.809869931071428

 $00{:}22{:}29.640 \dashrightarrow 00{:}22{:}31.944$ in blue are the ones that Channel

NOTE Confidence: 0.809869931071428

 $00{:}22{:}31{.}944 \dashrightarrow 00{:}22{:}33{.}724$ the sulfur to the biosynthesis.

NOTE Confidence: 0.809869931071428

 $00:22:33.730 \longrightarrow 00:22:34.942$ So for example,

00:22:34.942 --> 00:22:38.682 if you delete a you get a very distinct

NOTE Confidence: 0.809869931071428

 $00:22:38.682 \rightarrow 00:22:41.154$ phenotype that is a deficiency of

NOTE Confidence: 0.809869931071428

 $00:22:41.154 \rightarrow 00:22:43.788$ two pyridine and deficiency of MOCO.

NOTE Confidence: 0.809869931071428

 $00:22:43.790 \rightarrow 00:22:45.794$ But you don't affect other pathways

NOTE Confidence: 0.809869931071428

 $00{:}22{:}45.794 \dashrightarrow 00{:}22{:}47.811$ in reality actually affect a little

NOTE Confidence: 0.809869931071428

 $00{:}22{:}47.811 \dashrightarrow 00{:}22{:}49.683$ bit because you are disrupting the

NOTE Confidence: 0.809869931071428

 $00:22:49.683 \longrightarrow 00:22:51.228$ equilibrium or so for transfer.

NOTE Confidence: 0.809869931071428

00:22:51.230 --> 00:22:52.178 So you actually.

NOTE Confidence: 0.809869931071428

 $00{:}22{:}52{.}178 \dashrightarrow 00{:}22{:}54{.}074$ That boost on iron sulfur production

NOTE Confidence: 0.809869931071428

 $00:22:54.074 \rightarrow 00:22:55.825$ because you don't have that

NOTE Confidence: 0.809869931071428

 $00:22:55.825 \rightarrow 00:22:56.515$ competition anymore?

NOTE Confidence: 0.729175663448276

 $00{:}22{:}58.670 \dashrightarrow 00{:}23{:}01.246$ What we found, you know very early stages

NOTE Confidence: 0.729175663448276

 $00{:}23{:}01{.}246 \dashrightarrow 00{:}23{:}04{.}738$ when I when I joined Wake Forest is that

NOTE Confidence: 0.729175663448276

00:23:04.738 --> 00:23:06.717 Bacillus subtilis doesn't contain one

NOTE Confidence: 0.729175663448276

 $00{:}23{:}06{.}717 \dashrightarrow 00{:}23{:}09{.}223$ Sistine the sulfur is it contains 4.

NOTE Confidence: 0.729175663448276

 $00:23:09.230 \longrightarrow 00:23:13.642$ So that to us already told that you

 $00{:}23{:}13.642 \dashrightarrow 00{:}23{:}15.718$ know some of those pathways were

NOTE Confidence: 0.729175663448276

 $00{:}23{:}15{.}718 \dashrightarrow 00{:}23{:}18{.}205$ different and then by looking at the

NOTE Confidence: 0.729175663448276

 $00:23:18.205 \rightarrow 00:23:20.491$ genome neighborhood we could get some

NOTE Confidence: 0.729175663448276

 $00:23:20.491 \rightarrow 00:23:22.455$ insight about their physiological

NOTE Confidence: 0.729175663448276

 $00:23:22.455 \rightarrow 00:23:24.910$ functions in their particular Organism.

NOTE Confidence: 0.729175663448276

 $00{:}23{:}24{.}910 \dashrightarrow 00{:}23{:}27{.}520$ So so far in my lab and also others

NOTE Confidence: 0.729175663448276

 $00:23:27.520 \longrightarrow 00:23:28.659$ in the field.

NOTE Confidence: 0.729175663448276

 $00{:}23{:}28.660 \dashrightarrow 00{:}23{:}32.149$ Have been able to demonstrate the

NOTE Confidence: 0.729175663448276

 $00{:}23{:}32{.}149 \dashrightarrow 00{:}23{:}34{.}065$ partnership between assisting the

NOTE Confidence: 0.729175663448276

00:23:34.065 --> 00:23:36.460 Sofras and they're still perceptor

NOTE Confidence: 0.729175663448276

 $00:23:36.526 \rightarrow 00:23:38.521$ and validate their proposed roles

NOTE Confidence: 0.729175663448276

 $00{:}23{:}38{.}521 \dashrightarrow 00{:}23{:}41{.}050$ in the centers of tailcoat factor.

NOTE Confidence: 0.729175663448276

 $00{:}23{:}41{.}050 \dashrightarrow 00{:}23{:}43{.}546$ So I have done work in some of

NOTE Confidence: 0.729175663448276

 $00{:}23{:}43.546 \dashrightarrow 00{:}23{:}45.429$ those all those proteins,

NOTE Confidence: 0.729175663448276

 $00{:}23{:}45{.}430 \dashrightarrow 00{:}23{:}48{.}386$ but what I'm going to concentrate the

00:23:48.386 --> 00:23:52.132 talk it's on wire VO&MA they're they're

NOTE Confidence: 0.729175663448276

 $00:23:52.132 \rightarrow 00:23:55.336$ relevant for two though you're adding.

NOTE Confidence: 0.729175663448276

 $00{:}23{:}55{.}340 \dashrightarrow 00{:}23{:}56{.}428$ So as a biochemist,

NOTE Confidence: 0.729175663448276

 $00:23:56.428 \rightarrow 00:23:58.540$ the first thing that we do is

NOTE Confidence: 0.729175663448276

 $00{:}23{:}58{.}540 \dashrightarrow 00{:}24{:}00{.}640$ actually isolate the existing the

NOTE Confidence: 0.729175663448276

 $00{:}24{:}00{.}640 \dashrightarrow 00{:}24{:}02{.}320$ Selfridge perform enzyme kinetics.

NOTE Confidence: 0.729175663448276

 $00{:}24{:}02{.}320 \dashrightarrow 00{:}24{:}04{.}630$ And some of those initial studies

NOTE Confidence: 0.729175663448276

 $00{:}24{:}04{.}630 \dashrightarrow 00{:}24{:}07{.}305$ show very clearly that those enzymes

NOTE Confidence: 0.729175663448276

 $00:24:07.305 \longrightarrow 00:24:09.960$ display very distinct kinetic behaviors.

NOTE Confidence: 0.729175663448276

 $00:24:09.960 \rightarrow 00:24:11.490$ What it was really interesting.

NOTE Confidence: 0.729175663448276

 $00{:}24{:}11{.}490 \dashrightarrow 00{:}24{:}14{.}166$ So those initial as says were done

NOTE Confidence: 0.729175663448276

 $00:24:14.166 \longrightarrow 00:24:17.163$ like most people in the field do.

NOTE Confidence: 0.729175663448276

 $00:24:17.163 \longrightarrow 00:24:19.341$ So everybody at that point would

NOTE Confidence: 0.729175663448276

00:24:19.341 --> 00:24:21.389 do just have kinetic reactions

NOTE Confidence: 0.729175663448276

 $00:24:21.389 \rightarrow 00:24:24.017$ where you react with sustain and

NOTE Confidence: 0.729175663448276

 $00:24:24.017 \rightarrow 00:24:26.228$ then you measure the half.
- NOTE Confidence: 0.729175663448276
- $00:24:26.230 \longrightarrow 00:24:28.273$ Reaction rate through
- NOTE Confidence: 0.729175663448276
- $00:24:28.273 \longrightarrow 00:24:30.316$ quantification of sulfide.
- NOTE Confidence: 0.805517600625
- $00:24:32.610 \longrightarrow 00:24:35.753$ What we wanted to do is then
- NOTE Confidence: 0.805517600625
- $00{:}24{:}35{.}753 \dashrightarrow 00{:}24{:}38{.}539$ demonstrate that the presence of
- NOTE Confidence: 0.805517600625
- $00{:}24{:}38{.}539 \dashrightarrow 00{:}24{:}41{.}227$ the physiological sofa receptor,
- NOTE Confidence: 0.805517600625
- $00:24:41.230 \longrightarrow 00:24:43.474$ so the second service trading this
- NOTE Confidence: 0.805517600625
- $00{:}24{:}43{.}474 \dashrightarrow 00{:}24{:}46{.}510$ reaction was a valid SOFA receptor.
- NOTE Confidence: 0.805517600625
- $00:24:46.510 \rightarrow 00:24:48.466$ And then in this particular case,
- NOTE Confidence: 0.805517600625
- $00:24:48.470 \longrightarrow 00:24:50.990$ the reaction rate in the presence
- NOTE Confidence: 0.805517600625
- $00{:}24{:}50{.}990 \dashrightarrow 00{:}24{:}53{.}258$ of the sulfur acceptor enhanced
- NOTE Confidence: 0.805517600625
- 00:24:53.258 --> 00:24:55.298 about over a hundredfold,
- NOTE Confidence: 0.805517600625
- $00{:}24{:}55{.}300 \dashrightarrow 00{:}24{:}58{.}268$ so indicating that the sulfur here in
- NOTE Confidence: 0.805517600625
- $00{:}24{:}58{.}268 \dashrightarrow 00{:}25{:}01{.}879$ this case was much better in abstracting.
- NOTE Confidence: 0.805517600625
- $00{:}25{:}01{.}880 \dashrightarrow 00{:}25{:}04{.}308$ The personal file then
- NOTE Confidence: 0.805517600625
- $00:25:04.308 \longrightarrow 00:25:06.129$ an artificial reductant.
- NOTE Confidence: 0.8653921

 $00{:}25{:}08{.}250 \dashrightarrow 00{:}25{:}08{.}870$ Sure.

NOTE Confidence: 0.2021982

 $00{:}25{:}10{.}980 \dashrightarrow 00{:}25{:}11{.}440$ Reaction.

NOTE Confidence: 0.69554375

 $00:25:15.140 \longrightarrow 00:25:17.650$ Yes, you.

NOTE Confidence: 0.768738014583333

 $00{:}25{:}20{.}270 \dashrightarrow 00{:}25{:}22{.}662$ Yeah. So you may want to think there

NOTE Confidence: 0.768738014583333

 $00:25:22.662 \longrightarrow 00:25:25.110$ are very high but the intracellular

NOTE Confidence: 0.768738014583333

 $00{:}25{:}25{.}110 \dashrightarrow 00{:}25{:}27{.}335$ level concentration on reduce this

NOTE Confidence: 0.768738014583333

 $00:25:27.335 \longrightarrow 00:25:30.602$ thing in the cells of his 68 micromolar.

NOTE Confidence: 0.768738014583333

 $00:25:30.602 \rightarrow 00:25:34.690$ So actually that's actually quite nice if

NOTE Confidence: 0.768738014583333

00:25:34.795 --> 00:25:38.820 you study kind of like metabolism because

NOTE Confidence: 0.768738014583333

 $00{:}25{:}38{.}820 \dashrightarrow 00{:}25{:}42{.}527$ most enzymes they kind of operate around

NOTE Confidence: 0.768738014583333

 $00{:}25{:}42.527 \dashrightarrow 00{:}25{:}45.228$ the KM that they they have you know.

NOTE Confidence: 0.768738014583333

 $00{:}25{:}45{.}230 \dashrightarrow 00{:}25{:}48{.}093$ So if the concentration is it OK

NOTE Confidence: 0.768738014583333

 $00{:}25{:}48.093 \dashrightarrow 00{:}25{:}50.779$ that allows the cells to adjust.

NOTE Confidence: 0.768738014583333

 $00:25:50.780 \rightarrow 00:25:53.167$ The velocity of that reaction because they

NOTE Confidence: 0.768738014583333

 $00{:}25{:}53{.}167 \dashrightarrow 00{:}25{:}55{.}497$ are operating around KM and that's the case.

NOTE Confidence: 0.768738014583333

 $00:25:55.500 \rightarrow 00:25:57.390$ But one thing that you may,

- NOTE Confidence: 0.768738014583333
- $00:25:57.390 \longrightarrow 00:26:00.414$ you know, kind of notice is that the
- NOTE Confidence: 0.768738014583333
- $00:26:00.414 \rightarrow 00:26:03.058$ lowest KM here is for a wire VO.
- NOTE Confidence: 0.768738014583333
- $00:26:03.060 \rightarrow 00:26:05.052$ You know one thing that we may want
- NOTE Confidence: 0.768738014583333
- $00:26:05.052 \rightarrow 00:26:06.887$ to postulate like because this enzyme
- NOTE Confidence: 0.768738014583333
- $00{:}26{:}06{.}887 \dashrightarrow 00{:}26{:}08{.}813$ is so essential in this modification,
- NOTE Confidence: 0.768738014583333
- $00{:}26{:}08.820 \dashrightarrow 00{:}26{:}11.334$ so essential maybe the enzyme has
- NOTE Confidence: 0.768738014583333
- $00{:}26{:}11.334 \dashrightarrow 00{:}26{:}14.294$ evolved to have a really low KM
- NOTE Confidence: 0.768738014583333
- $00:26:14.294 \longrightarrow 00:26:16.294$ to give a preference for,
- NOTE Confidence: 0.768738014583333
- $00{:}26{:}16.300 \dashrightarrow 00{:}26{:}18.664$ so for mobilization on that pathway
- NOTE Confidence: 0.768738014583333
- $00:26:18.664 \longrightarrow 00:26:20.240$ under conditions that sulfur
- NOTE Confidence: 0.768738014583333
- $00:26:20.301 \rightarrow 00:26:21.837$ is not readily available.
- NOTE Confidence: 0.880771825
- $00{:}26{:}25{.}240 \dashrightarrow 00{:}26{:}26{.}608$ No, no, that's great.
- NOTE Confidence: 0.5226583
- 00:26:29.520 --> 00:26:30.010 Guys.
- NOTE Confidence: 0.5839956
- 00:26:32.450 --> 00:26:32.770 Top.
- NOTE Confidence: 0.780740590666667
- $00:26:39.740 \longrightarrow 00:26:41.168$ Not this enzyme.
- NOTE Confidence: 0.7807405906666667

 $00:26:41.168 \rightarrow 00:26:44.024$ The next enzyme on the pathways

NOTE Confidence: 0.780740590666667

 $00{:}26{:}44.024 \dashrightarrow 00{:}26{:}46.717$ coupled to the hydrolysis of ATP?

NOTE Confidence: 0.780740590666667

 $00:26:46.720 \longrightarrow 00:26:50.160$ Yeah, not, not this particular.

NOTE Confidence: 0.7807405906666667

00:26:50.160 - 00:26:52.636 Not any assistant sufferers.

NOTE Confidence: 0.7807405906666667

 $00:26:52.636 \rightarrow 00:26:57.040$ They use POP chemistry to dissolve urate.

NOTE Confidence: 0.7807405906666667

 $00{:}26{:}57{.}040 \dashrightarrow 00{:}26{:}59{.}992$ And we have done, I have not included

NOTE Confidence: 0.7807405906666667

 $00{:}26{:}59{.}992 \dashrightarrow 00{:}27{:}01{.}953$ here extensive kinetic analysis to

NOTE Confidence: 0.7807405906666667

 $00:27:01.953 \rightarrow 00:27:05.105$ show this is a ping pong mechanism and

NOTE Confidence: 0.780740590666667

 $00{:}27{:}05{.}105 \dashrightarrow 00{:}27{:}07{.}475$ the formation of the personal fide.

NOTE Confidence: 0.7807405906666667

00:27:07.480 --> 00:27:10.500 It's a mandatory staff.

NOTE Confidence: 0.7807405906666667

 $00:27:10.500 \rightarrow 00:27:12.068$ So as you imagine,

NOTE Confidence: 0.7807405906666667

 $00:27:12.068 \longrightarrow 00:27:14.420$ there's a kinetic burst in the

NOTE Confidence: 0.7807405906666667

 $00:27:14.500 \longrightarrow 00:27:16.860$ absence of the Super receptor

NOTE Confidence: 0.7807405906666667

 $00:27:16.860 \rightarrow 00:27:19.700$ and then this enzyme actually can

NOTE Confidence: 0.7807405906666667

 $00:27:19.700 \longrightarrow 00:27:22.100$ slowly decay to turn over here,

NOTE Confidence: 0.7807405906666667

 $00:27:22.100 \longrightarrow 00:27:24.128$ but the presence of the software

- NOTE Confidence: 0.7807405906666667
- $00:27:24.128 \rightarrow 00:27:25.933$ sapter enhances over 100 fold
- NOTE Confidence: 0.7807405906666667
- $00:27:25.933 \longrightarrow 00:27:27.497$ the overall catalytic cycle.
- NOTE Confidence: 0.668682785
- 00:27:34.510 --> 00:27:39.170 Periodic cells. Similar.
- NOTE Confidence: 0.668682785
- $00:27:39.170 \longrightarrow 00:27:41.290$ Yeah, it could excel.
- NOTE Confidence: 0.668682785
- $00{:}27{:}41{.}290 \dashrightarrow 00{:}27{:}44{.}470$ So sisting the cell phrase activity,
- NOTE Confidence: 0.668682785
- $00:27:44.470 \longrightarrow 00:27:47.310$ it's confined to the mitochondria,
- NOTE Confidence: 0.668682785
- $00:27:47.310 \longrightarrow 00:27:48.770$ so there's only one gene.
- NOTE Confidence: 0.668682785
- $00{:}27{:}48.770 \dashrightarrow 00{:}27{:}51.444$ And FS1, the activity of this enzyme
- NOTE Confidence: 0.668682785
- $00{:}27{:}51{.}444 \dashrightarrow 00{:}27{:}53{.}950$ is confined to the mitochondria.
- NOTE Confidence: 0.668682785
- 00:27:53.950 --> 00:27:54.766 And interestingly,
- NOTE Confidence: 0.668682785
- $00:27:54.766 \rightarrow 00:27:57.622$ the reactivity of this enzyme is highly
- NOTE Confidence: 0.668682785
- 00:27:57.622 --> 00:28:00.358 dependent on the presence of the sulfur
- NOTE Confidence: 0.668682785
- 00:28:00.358 --> 00:28:01.870 acceptor and modulating proteins.
- NOTE Confidence: 0.668682785
- $00{:}28{:}01{.}870 \dashrightarrow 00{:}28{:}04{.}770$ So there's a sulfur mobilization
- NOTE Confidence: 0.668682785
- $00{:}28{:}04.770 \dashrightarrow 00{:}28{:}07.440$ just coupled to iron metabolism.
- NOTE Confidence: 0.668682785

- $00:28:07.440 \longrightarrow 00:28:09.300$ So there's a protein.
- NOTE Confidence: 0.668682785
- $00:28:09.300 \longrightarrow 00:28:11.200$ It's called for taxing the
- NOTE Confidence: 0.668682785
- $00:28:11.200 \longrightarrow 00:28:12.720$ binds to the sustained,
- NOTE Confidence: 0.668682785
- $00:28:12.720 \rightarrow 00:28:15.261$ the suffrage and the binding of the
- NOTE Confidence: 0.668682785
- 00:28:15.261 --> 00:28:17.855 fratax
in to the assisting the surfaces
- NOTE Confidence: 0.668682785
- 00:28:17.855 --> 00:28:20.705 enhances the rate of sulfur transfer.
- NOTE Confidence: 0.668682785
- $00{:}28{:}20{.}710 \dashrightarrow 00{:}28{:}24{.}598$ And then what it's new now is that.
- NOTE Confidence: 0.668682785
- $00:28:24.600 \rightarrow 00:28:26.160$ This reaction is dependent on
- NOTE Confidence: 0.668682785
- $00{:}28{:}26.160 \dashrightarrow 00{:}28{:}27.720$ the SOFA receptor where iron
- NOTE Confidence: 0.668682785
- $00:28:27.778 \rightarrow 00:28:29.338$ sulfur clusters you're bound.
- NOTE Confidence: 0.668682785
- $00{:}28{:}29{.}340 \dashrightarrow 00{:}28{:}31{.}800$ So relevant for pathological behaviors
- NOTE Confidence: 0.668682785
- $00:28:31.800 \longrightarrow 00:28:34.879$ is there's a disease that's called
- NOTE Confidence: 0.668682785
- 00:28:34.879 --> 00:28:37.055 Fredericks at axia that's associated
- NOTE Confidence: 0.668682785
- $00:28:37.055 \rightarrow 00:28:39.775$ with mutations in the FRATAXIN
- NOTE Confidence: 0.668682785
- $00:28:39.852 \rightarrow 00:28:42.580$ gene and that disrupts not only
- NOTE Confidence: 0.668682785
- $00{:}28{:}42.580 \dashrightarrow 00{:}28{:}45.010$ iron sulfur metabolism but also

- NOTE Confidence: 0.668682785
- $00{:}28{:}45.094 \dashrightarrow 00{:}28{:}47.858$ disrupts iron metabolism overall.
- NOTE Confidence: 0.668682785
- $00:28:47.860 \longrightarrow 00:28:50.020$ So mutation for taxing leads to
- NOTE Confidence: 0.668682785
- $00{:}28{:}50{.}020 \dashrightarrow 00{:}28{:}51{.}825$ mitochondrial iron overload at the
- NOTE Confidence: 0.668682785
- $00:28:51.825 \rightarrow 00:28:53.960$ same time you have all the phenotypes.
- NOTE Confidence: 0.668682785
- $00{:}28{:}53{.}960 \dashrightarrow 00{:}28{:}55{.}884$ Associated with iron deficiency
- NOTE Confidence: 0.668682785
- $00{:}28{:}55{.}884 \dashrightarrow 00{:}28{:}58{.}289$ because you are not channeling
- NOTE Confidence: 0.668682785
- $00:28:58.289 \rightarrow 00:29:00.655$ the iron to the proper places.
- NOTE Confidence: 0.668682785
- 00:29:00.655 --> 00:29:03.625 Maybe just deviating, but you know,
- NOTE Confidence: 0.668682785
- $00:29:03.630 \rightarrow 00:29:05.840$ hopefully that answers your question.
- NOTE Confidence: 0.668682785
- 00:29:05.840 --> 00:29:08.620 Yeah, OK.
- NOTE Confidence: 0.668682785
- $00:29:08.620 \rightarrow 00:29:11.098$ So what it's quite interesting is
- NOTE Confidence: 0.668682785
- $00{:}29{:}11.098 \dashrightarrow 00{:}29{:}13.268$ that those super receptor molecules
- NOTE Confidence: 0.668682785
- $00:29:13.268 \longrightarrow 00:29:15.060$ are quite as specific,
- NOTE Confidence: 0.668682785
- $00{:}29{:}15{.}060 \dashrightarrow 00{:}29{:}15{.}433$ right.
- NOTE Confidence: 0.668682785
- $00:29:15.433 \longrightarrow 00:29:17.671$ So you have this protein here
- NOTE Confidence: 0.668682785

00:29:17.671 -> 00:29:19.870 stuff view then we have shown

NOTE Confidence: 0.668682785

 $00{:}29{:}19{.}870 \dashrightarrow 00{:}29{:}21{.}880$ that in the zinc bound form,

NOTE Confidence: 0.668682785

00:29:21.880 --> 00:29:23.440 so tightly bound zinc,

NOTE Confidence: 0.668682785

 $00:29:23.440 \rightarrow 00:29:26.329$ so the presence of so few enhances

NOTE Confidence: 0.668682785

 $00:29:26.329 \longrightarrow 00:29:29.598$ the activity of its partners so fast,

NOTE Confidence: 0.668682785

 $00:29:29.600 \longrightarrow 00:29:32.928$ but so few is not able to display

NOTE Confidence: 0.668682785

 $00:29:32.928 \rightarrow 00:29:35.258$ similar behavior to other systems,

NOTE Confidence: 0.668682785

 $00:29:35.260 \longrightarrow 00:29:37.320$ the surfaces in Basilius as

NOTE Confidence: 0.668682785

 $00{:}29{:}37{.}320 \dashrightarrow 00{:}29{:}38{.}556$ well as orthologs.

NOTE Confidence: 0.668682785

 $00:29:38.560 \longrightarrow 00:29:40.842$ Listing to sell for race for him

NOTE Confidence: 0.668682785

 $00{:}29{:}40.842 \dashrightarrow 00{:}29{:}43.052$ to note here those enzymes are

NOTE Confidence: 0.668682785

00:29:43.052 --> 00:29:45.356 extremely similar so the E coli

NOTE Confidence: 0.668682785

 $00{:}29{:}45{.}356 \dashrightarrow 00{:}29{:}47{.}669$ SUV S and Bacillus sub S they

NOTE Confidence: 0.668682785

 $00:29:47.669 \rightarrow 00:29:50.423$ are over 60% identity identical,

NOTE Confidence: 0.668682785

 $00{:}29{:}50{.}423 \dashrightarrow 00{:}29{:}54{.}689$ yet they cannot cross react so.

NOTE Confidence: 0.668682785

 $00:29:54.690 \rightarrow 00:29:57.162$ And and that's something that it's

- NOTE Confidence: 0.668682785
- $00:29:57.162 \longrightarrow 00:29:59.288$ an important feature of those
- NOTE Confidence: 0.668682785
- $00{:}29{:}59{.}288 \dashrightarrow 00{:}30{:}01{.}278$ enzymes to guarantee that the
- NOTE Confidence: 0.668682785
- $00:30:01.278 \longrightarrow 00:30:03.842$ sulfur is channel to the proper
- NOTE Confidence: 0.668682785
- $00:30:03.842 \rightarrow 00:30:06.077$ pathway that you were recruiting.
- NOTE Confidence: 0.668682785
- 00:30:06.080 --> 00:30:08.260 Umm.
- NOTE Confidence: 0.668682785
- $00:30:08.260 \longrightarrow 00:30:10.522$ So that's not only a specific
- NOTE Confidence: 0.668682785
- $00:30:10.522 \longrightarrow 00:30:12.030$ feature of self fast.
- NOTE Confidence: 0.668682785
- $00:30:12.030 \longrightarrow 00:30:14.490$ So this wire the operating that
- NOTE Confidence: 0.668682785
- $00:30:14.490 \longrightarrow 00:30:16.618$ we we eventually postulated the
- NOTE Confidence: 0.668682785
- 00:30:16.618 --> 00:30:18.703 dead it's involving 2 pyridine
- NOTE Confidence: 0.668682785
- $00:30:18.703 \longrightarrow 00:30:21.051$ has its activity enhanced by the
- NOTE Confidence: 0.668682785
- 00:30:21.051 --> 00:30:23.186 presence of ATP and then we know
- NOTE Confidence: 0.668682785
- $00{:}30{:}23.186 \dashrightarrow 00{:}30{:}25.440$ that the catalytic competent form
- NOTE Confidence: 0.668682785
- $00:30:25.440 \longrightarrow 00:30:28.863$ of 80 of MDMA that's higher delays
- NOTE Confidence: 0.668682785
- $00:30:28.863 \longrightarrow 00:30:30.958$ is the ATP bound form.
- NOTE Confidence: 0.668682785

 $00:30:30.960 \longrightarrow 00:30:34.533$ So the enzyme has to have ATP bound to

NOTE Confidence: 0.668682785

 $00{:}30{:}34{.}533 \dashrightarrow 00{:}30{:}38{.}517$ be able to receive the sulfur and then.

NOTE Confidence: 0.668682785

 $00{:}30{:}38{.}520 \dashrightarrow 00{:}30{:}42{.}235$ Follow the chemical reaction so we

NOTE Confidence: 0.668682785

 $00:30:42.235 \rightarrow 00:30:44.618$ know that this happens out again

NOTE Confidence: 0.668682785

 $00:30:44.618 \rightarrow 00:30:47.234$ through formation of a personal fight.

NOTE Confidence: 0.668682785

 $00:30:47.240 \rightarrow 00:30:49.292$ Intermedia using those labeling

NOTE Confidence: 0.668682785

 $00:30:49.292 \longrightarrow 00:30:51.344$ so for 35 assays.

NOTE Confidence: 0.834499641333334

00:30:53.890 - > 00:30:55.778 What we also know is that you know

NOTE Confidence: 0.834499641333334

 $00:30:55.778 \rightarrow 00:30:58.161$ what we are doing in vitro reactions is

NOTE Confidence: 0.834499641333334

 $00:30:58.161 \rightarrow 00:31:00.186$ important to be mindful and critical

NOTE Confidence: 0.834499641333334

 $00{:}31{:}00{.}186 \dashrightarrow 00{:}31{:}02{.}376$ about the reaction conditions and then

NOTE Confidence: 0.834499641333334

 $00{:}31{:}02{.}376 \dashrightarrow 00{:}31{:}04{.}745$ whether those reaction conditions mimic

NOTE Confidence: 0.834499641333334

 $00:31:04.745 \dashrightarrow 00:31:07.470$ physiological conditions in the cell.

NOTE Confidence: 0.834499641333334

00:31:07.470 --> 00:31:09.274 So like I mentioned,

NOTE Confidence: 0.834499641333334

 $00:31:09.274 \rightarrow 00:31:11.980$ the field is populated with publications

NOTE Confidence: 0.834499641333334

 $00{:}31{:}12.063 \dashrightarrow 00{:}31{:}14.604$ that use DT and that provides a

 $00:31:14.604 \rightarrow 00:31:17.099$ means to quantify reaction products.

NOTE Confidence: 0.834499641333334

 $00{:}31{:}17.100 \dashrightarrow 00{:}31{:}21.510$ So DT is none are available in the cell.

NOTE Confidence: 0.834499641333334

 $00:31:21.510 \longrightarrow 00:31:23.190$ So most cells use glucose.

NOTE Confidence: 0.834499641333334

 $00:31:23.190 \longrightarrow 00:31:25.854$ I also the activity of those

NOTE Confidence: 0.834499641333334

 $00:31:25.854 \rightarrow 00:31:28.750$ enzymes in the presence of mutation.

NOTE Confidence: 0.834499641333334

00:31:28.750 --> 00:31:30.337 It's very distinct,

NOTE Confidence: 0.834499641333334

 $00:31:30.337 \rightarrow 00:31:34.040$ yet you can see an enhancement here.

NOTE Confidence: 0.834499641333334

 $00:31:34.040 \longrightarrow 00:31:35.328$ Tell us uh so.

NOTE Confidence: 0.834499641333334

00:31:35.328 --> 00:31:36.938 But Tillis doesn't use glutathione,

NOTE Confidence: 0.834499641333334

 $00:31:36.940 \rightarrow 00:31:38.440$ doesn't make glutathione instead

NOTE Confidence: 0.834499641333334

 $00:31:38.440 \longrightarrow 00:31:40.690$ uses basically PIOS or have a

NOTE Confidence: 0.834499641333334

 $00{:}31{:}40.759 \dashrightarrow 00{:}31{:}42.759$ collaborator in my department that

NOTE Confidence: 0.834499641333334

 $00{:}31{:}42.759 \dashrightarrow 00{:}31{:}44.759$ synthesize facility file for me

NOTE Confidence: 0.834499641333334

00:31:44.760 --> 00:31:47.852 facility always a very poor reduction

NOTE Confidence: 0.834499641333334

 $00:31:47.852 \dashrightarrow 00:31:50.736$ is even inhibits the reaction in DT.

 $00:31:50.740 \longrightarrow 00:31:54.085$ But pyridoxine is a quite

NOTE Confidence: 0.834499641333334

 $00:31:54.085 \rightarrow 00:31:56.092$ effective personified reductase

NOTE Confidence: 0.834499641333334

 $00:31:56.092 \rightarrow 00:32:00.760$ and enhances greatly the rate of a

NOTE Confidence: 0.834499641333334

 $00:32:00.760 \rightarrow 00:32:03.320$ personified formation and reduction.

NOTE Confidence: 0.834499641333334

 $00:32:03.320 \dashrightarrow 00:32:06.380$ And this is staff, but not at this is staff.

NOTE Confidence: 0.834499641333334

 $00{:}32{:}06{.}380 \dashrightarrow 00{:}32{:}08{.}168$ So that's what we think it's

NOTE Confidence: 0.834499641333334

00:32:08.168 --> 00:32:09.360 happening in the cell.

NOTE Confidence: 0.834499641333334

 $00:32:09.360 \rightarrow 00:32:13.257$ This is not a unique feature of wire VOC

NOTE Confidence: 0.834499641333334

 $00:32:13.260 \rightarrow 00:32:16.316$ reactions done with stuff you and so fast.

NOTE Confidence: 0.834499641333334

 $00:32:16.320 \longrightarrow 00:32:19.128$ Also show that in the kinetic

NOTE Confidence: 0.834499641333334

 $00:32:19.128 \dashrightarrow 00:32:22.001$ profile here indicates that the rate

NOTE Confidence: 0.834499641333334

00:32:22.001 --> 00:32:24.296 of sulfur mobilization is coupled

NOTE Confidence: 0.834499641333334

 $00{:}32{:}24.296 \dashrightarrow 00{:}32{:}27.348$ with the rate of sulfur reduction

NOTE Confidence: 0.834499641333334

 $00:32:27.348 \longrightarrow 00:32:29.460$ on those kinetic schemes.

NOTE Confidence: 0.834499641333334

 $00{:}32{:}29{.}460 \dashrightarrow 00{:}32{:}31{.}692$ So next what we wanted to do it's

NOTE Confidence: 0.834499641333334

 $00:32:31.692 \rightarrow 00:32:33.846$ kind of replicate what we're seeing

 $00:32:33.846 \longrightarrow 00:32:36.364$ in vivo or at least what we are

NOTE Confidence: 0.834499641333334

 $00:32:36.364 \longrightarrow 00:32:38.660$ postulating in in vivo that can we.

NOTE Confidence: 0.834499641333334

 $00{:}32{:}38.660 \dashrightarrow 00{:}32{:}41.150$ So we know establish that where

NOTE Confidence: 0.834499641333334

 $00:32:41.150 \longrightarrow 00:32:43.617$ there was assisting the self rays

NOTE Confidence: 0.834499641333334

 $00{:}32{:}43.617 \dashrightarrow 00{:}32{:}46.151$ and then imma is a sulfa receptor

NOTE Confidence: 0.834499641333334

00:32:46.151 --> 00:32:48.257 here in the ATP bound form.

NOTE Confidence: 0.834499641333334

 $00{:}32{:}48.260 \dashrightarrow 00{:}32{:}51.036$ So next we wanted to proceed on the

NOTE Confidence: 0.834499641333334

 $00:32:51.036 \rightarrow 00:32:53.355$ pathway and validate it and then in

NOTE Confidence: 0.834499641333334

 $00{:}32{:}53{.}355 \dashrightarrow 00{:}32{:}56{.}064$ May it's in fact a tire regulates that

NOTE Confidence: 0.834499641333334

 $00{:}32{:}56{.}064 \dashrightarrow 00{:}32{:}59{.}983$ can pass on the sulfur to the tier and a.

NOTE Confidence: 0.834499641333334

 $00{:}32{:}59{.}983 \dashrightarrow 00{:}33{:}02{.}725$ So the reaction that is proposed here is

NOTE Confidence: 0.834499641333334

 $00{:}33{:}02.725 \dashrightarrow 00{:}33{:}05.069$ that in the first step of the reaction,

NOTE Confidence: 0.834499641333334

00:33:05.070 --> 00:33:07.828 so in uridine you typically have oxygen NOTE Confidence: 0.834499641333334

 $00:33:07.828 \longrightarrow 00:33:10.949$ here which is not a good leaving group.

NOTE Confidence: 0.834499641333334

 $00{:}33{:}10{.}950 \dashrightarrow 00{:}33{:}13{.}342$ So the first step on the reaction is

 $00:33:13.342 \longrightarrow 00:33:15.527$ that ventilate the uridine acquisition 2.

NOTE Confidence: 0.834499641333334

 $00:33:15.530 \rightarrow 00:33:18.498$ So the sulfur can directly attack leading

NOTE Confidence: 0.834499641333334

 $00:33:18.498 \rightarrow 00:33:21.168$ to the formation of a tooth iodine.

NOTE Confidence: 0.834499641333334

 $00:33:21.170 \rightarrow 00:33:24.047$ So when we have done those experiments,

NOTE Confidence: 0.834499641333334

 $00:33:24.050 \rightarrow 00:33:28.030$ yes we can form 2 pyridine in the test tube.

NOTE Confidence: 0.834499641333334

 $00:33:28.030 \longrightarrow 00:33:29.980$ So validating that this is.

NOTE Confidence: 0.834499641333334

 $00:33:29.980 \longrightarrow 00:33:31.404$ As A2 pathway component,

NOTE Confidence: 0.834499641333334

 $00:33:31.404 \rightarrow 00:33:33.540$ you don't need all the seven

NOTE Confidence: 0.834499641333334

 $00{:}33{:}33{.}610 \dashrightarrow 00{:}33{:}35{.}746$ components that we're seeing in E

NOTE Confidence: 0.834499641333334

 $00:33:35.746 \longrightarrow 00:33:38.293$ coli in the pathway is reliant on

NOTE Confidence: 0.834499641333334

 $00{:}33{:}38{.}293 \dashrightarrow 00{:}33{:}40{.}399$ the presence of a reducing agent.

NOTE Confidence: 0.834499641333334

 $00:33:40.400 \rightarrow 00:33:43.577$ So we don't know what step of it reducing

NOTE Confidence: 0.834499641333334

 $00{:}33{:}43.577 \dashrightarrow 00{:}33{:}45.851$ agent it's used but we postulated

NOTE Confidence: 0.834499641333334

 $00:33:45.851 \rightarrow 00:33:48.600$ it could be a desktop or desktop.

NOTE Confidence: 0.834499641333334

 $00{:}33{:}48.600 \dashrightarrow 00{:}33{:}51.057$ So you can have personal fight attacking

NOTE Confidence: 0.834499641333334

 $00{:}33{:}51{.}057 \dashrightarrow 00{:}33{:}53{.}695$ the other related or you can have a

- NOTE Confidence: 0.834499641333334
- $00:33:53.695 \rightarrow 00:33:55.595$ local reduction of that personal fight

 $00:33:55.595 \rightarrow 00:33:58.100$ so you have 3 sulfide attacking that.

NOTE Confidence: 0.834499641333334

00:33:58.100 --> 00:33:58.680 Nevertheless,

NOTE Confidence: 0.834499641333334

 $00:33:58.680 \dashrightarrow 00:34:03.320$ so we know and we can validate that

NOTE Confidence: 0.834499641333334

 $00:34:03.432 \rightarrow 00:34:06.807$ we can go from you to 2 or you.

NOTE Confidence: 0.834499641333334

 $00{:}34{:}06{.}810 \dashrightarrow 00{:}34{:}10{.}290$ But I also mentioned to you that this

NOTE Confidence: 0.834499641333334

 $00:34:10.290 \rightarrow 00:34:13.506$ modification occurs in conjunction

NOTE Confidence: 0.834499641333334

 $00:34:13.506 \rightarrow 00:34:16.330$ with a modification at A5 position.

NOTE Confidence: 0.805597788571429

 $00{:}34{:}16{.}330 \dashrightarrow 00{:}34{:}19{.}844$ So in this case M and M5 as as

NOTE Confidence: 0.805597788571429

 $00:34:19.844 \longrightarrow 00:34:22.553$ to you and in the literature was

NOTE Confidence: 0.805597788571429

 $00{:}34{:}22.553 \dashrightarrow 00{:}34{:}25.002$ proposed that those two pathways

NOTE Confidence: 0.805597788571429

 $00{:}34{:}25.002 \dashrightarrow 00{:}34{:}27.966$ were independent one to one another.

NOTE Confidence: 0.805597788571429

 $00:34:27.970 \longrightarrow 00:34:29.925$ So you could either titillate

NOTE Confidence: 0.805597788571429

 $00{:}34{:}29{.}925 \dashrightarrow 00{:}34{:}32{.}313$ your routine 1st and then you

NOTE Confidence: 0.805597788571429

 $00:34:32.313 \longrightarrow 00:34:34.449$ can modify the five position or

 $00:34:34.449 \rightarrow 00:34:36.869$ you can modify the five position.

NOTE Confidence: 0.805597788571429

 $00:34:36.870 \longrightarrow 00:34:38.750$ And then thiolate seconds.

NOTE Confidence: 0.805597788571429

 $00:34:38.750 \rightarrow 00:34:43.590$ So what we did here is that we use a T RNA,

NOTE Confidence: 0.805597788571429

 $00:34:43.590 \rightarrow 00:34:47.867$ a mixture of tyranny a that contain.

NOTE Confidence: 0.805597788571429

 $00{:}34{:}47.870 \dashrightarrow 00{:}34{:}51.356$ Unmodified you and partially modify you

NOTE Confidence: 0.805597788571429

 $00{:}34{:}51{.}356 \dashrightarrow 00{:}34{:}54{.}710$ and then we incubating the reaction

NOTE Confidence: 0.805597788571429

 $00{:}34{:}54{.}710 \dashrightarrow 00{:}34{:}57{.}986$ and to our surprise we're not able

NOTE Confidence: 0.805597788571429

 $00:34:57.986 \rightarrow 00:35:01.926$ to detect the synthesis of the fully

NOTE Confidence: 0.805597788571429

00:35:01.926 --> 00:35:06.290 modified M&
amp;
M as to you only to thy urity.

NOTE Confidence: 0.805597788571429

 $00:35:06.290 \rightarrow 00:35:08.980$ So that initial result suggested

NOTE Confidence: 0.805597788571429

 $00{:}35{:}08{.}980 \dashrightarrow 00{:}35{:}12{.}568$ that may be the pathways are non

NOTE Confidence: 0.805597788571429

 $00:35:12.568 \dashrightarrow 00:35:14.989$ independent bifurcated pathways,

NOTE Confidence: 0.805597788571429

 $00:35:14.990 \rightarrow 00:35:17.020$ maybe there was some sequentiality

NOTE Confidence: 0.805597788571429

 $00:35:17.020 \longrightarrow 00:35:18.238$ on that pathway.

NOTE Confidence: 0.805597788571429

 $00:35:18.240 \longrightarrow 00:35:21.828$ Somehow and then they was only

 $00:35:21.828 \rightarrow 00:35:24.220$ recognizing the unmodified view.

NOTE Confidence: 0.805597788571429

00:35:24.220 --> 00:35:26.570 Um, we?

NOTE Confidence: 0.805597788571429

 $00:35:26.570 \rightarrow 00:35:29.060$ Took advantage that the availability

NOTE Confidence: 0.805597788571429

00:35:29.060 --> 00:35:32.103 of a crystal structure of MMA

NOTE Confidence: 0.805597788571429

 $00{:}35{:}32{.}103 \dashrightarrow 00{:}35{:}34{.}476$ from an ortholog Organism that

NOTE Confidence: 0.805597788571429

00:35:34.476 - > 00:35:36.500 had the tyranny intermediate,

NOTE Confidence: 0.805597788571429

00:35:36.500 --> 00:35:37.430 adenylate intermediate.

NOTE Confidence: 0.805597788571429

 $00:35:37.430 \rightarrow 00:35:40.685$ So this is the position of distillation.

NOTE Confidence: 0.805597788571429

 $00{:}35{:}40.690 \dashrightarrow 00{:}35{:}43.298$ And so we look at the active side

NOTE Confidence: 0.805597788571429

 $00:35:43.298 \dashrightarrow 00:35:46.640$ and what it kind of kind of became

NOTE Confidence: 0.805597788571429

 $00:35:46.640 \longrightarrow 00:35:48.380$ a structured justification for

NOTE Confidence: 0.805597788571429

 $00:35:48.458 \longrightarrow 00:35:51.230$ our results is that are in close

NOTE Confidence: 0.805597788571429

 $00:35:51.230 \longrightarrow 00:35:53.878$ proximity here for this carbon 5

NOTE Confidence: 0.805597788571429

 $00:35:53.878 \rightarrow 00:35:56.794$ there was a concern venue alanine.

NOTE Confidence: 0.805597788571429

00:35:56.800 --> 00:35:57.172 Uh,

NOTE Confidence: 0.805597788571429

 $00{:}35{:}57{.}172 \dashrightarrow 00{:}35{:}59{.}776$ that kind of provide a rationale for

 $00:35:59.776 \rightarrow 00:36:02.032$ why this partially modified tier and

NOTE Confidence: 0.805597788571429

00:36:02.032 --> 00:36:05.140 a was not reacting to form 2 pyridine.

NOTE Confidence: 0.805597788571429

 $00{:}36{:}05{.}140 \dashrightarrow 00{:}36{:}08{.}116$ So we thought that the phenylalan ine

NOTE Confidence: 0.805597788571429

00:36:08.116 --> 00:36:10.496 was provided an historical hindrance

NOTE Confidence: 0.805597788571429

 $00{:}36{:}10.496 \dashrightarrow 00{:}36{:}12.849$ not restricting the partially modified

NOTE Confidence: 0.805597788571429

 $00{:}36{:}12.849 \dashrightarrow 00{:}36{:}14.754$ tyranny from entering the active

NOTE Confidence: 0.805597788571429

 $00:36:14.754 \longrightarrow 00:36:16.820$ side and getting tired related.

NOTE Confidence: 0.805597788571429

 $00:36:16.820 \longrightarrow 00:36:18.590$ So kind of the obvious experiment

NOTE Confidence: 0.805597788571429

 $00{:}36{:}18.590 \dashrightarrow 00{:}36{:}20.654$ is to mutate the enzyme and see

NOTE Confidence: 0.805597788571429

 $00:36:20.654 \rightarrow 00:36:22.558$ if we open up that active side.

NOTE Confidence: 0.805597788571429

 $00{:}36{:}22.560 \dashrightarrow 00{:}36{:}25.262$ Now we can feed a bigger substrate

NOTE Confidence: 0.805597788571429

 $00:36:25.262 \longrightarrow 00:36:27.284$ and that's exactly what we are

NOTE Confidence: 0.805597788571429

 $00{:}36{:}27.284 \dashrightarrow 00{:}36{:}28.148$ able to demonstrate.

NOTE Confidence: 0.805597788571429

 $00:36:28.150 \longrightarrow 00:36:33.802$ Is that mutant, so 55155 in Bacillus,

NOTE Confidence: 0.805597788571429

 $00:36:33.802 \longrightarrow 00:36:37.308$ 154 in E coli, but that's the residue.

 $00:36:37.308 \longrightarrow 00:36:40.706$ So if you open up now we can

NOTE Confidence: 0.805597788571429

00:36:40.706 --> 00:36:45.040 make M&M so the fully modified.

NOTE Confidence: 0.805597788571429

00:36:45.040 --> 00:36:46.820 Modification,

NOTE Confidence: 0.805597788571429

 $00:36:46.820 \longrightarrow 00:36:48.600$ right?

NOTE Confidence: 0.805597788571429

 $00{:}36{:}48.600 \dashrightarrow 00{:}36{:}51.102$ Using this variant form so those

NOTE Confidence: 0.805597788571429

 $00{:}36{:}51.102 \dashrightarrow 00{:}36{:}53.592$ results kind of postulate that at

NOTE Confidence: 0.805597788571429

 $00{:}36{:}53{.}592 \dashrightarrow 00{:}36{:}55{.}836$ least in the source of challenge

NOTE Confidence: 0.805597788571429

 $00:36:55.836 \dashrightarrow 00:36:57.928$ the pathway for modifications is

NOTE Confidence: 0.805597788571429

00:36:57.928 --> 00:37:00.472 sequential where you till late 1st

NOTE Confidence: 0.805597788571429

 $00:37:00.472 \longrightarrow 00:37:04.470$ and then you modify it A5 position.

NOTE Confidence: 0.805597788571429

 $00{:}37{:}04.470 \dashrightarrow 00{:}37{:}07.263$ So you know this work on devices

NOTE Confidence: 0.805597788571429

 $00{:}37{:}07{.}263 \dashrightarrow 00{:}37{:}09{.}438$ was very interesting and and

NOTE Confidence: 0.805597788571429

 $00{:}37{:}09{.}438 \dashrightarrow 00{:}37{:}11.693$ established that but still subtilis

NOTE Confidence: 0.805597788571429

 $00{:}37{:}11.693 \dashrightarrow 00{:}37{:}14.282$ uses a dedicated system to Socrates

NOTE Confidence: 0.805597788571429

 $00{:}37{:}14.282 \dashrightarrow 00{:}37{:}16.970$ and a SOFA receptor to violate a

NOTE Confidence: 0.805597788571429

 $00:37:16.970 \longrightarrow 00:37:20.282$ tyranna at the U34 position and

- NOTE Confidence: 0.805597788571429
- $00:37:20.282 \rightarrow 00:37:23.979$ what we thought here was that the.
- NOTE Confidence: 0.805597788571429
- $00:37:23.980 \rightarrow 00:37:26.040$ This distinctive reactivity provided
- NOTE Confidence: 0.805597788571429
- $00:37:26.040 \dashrightarrow 00:37:29.130$ sort of an opportunity for alternate
- NOTE Confidence: 0.805597788571429
- $00:37:29.200 \rightarrow 00:37:31.740$ regulation of the pathways involved,
- NOTE Confidence: 0.805597788571429
- $00{:}37{:}31{.}740 \dashrightarrow 00{:}37{:}33{.}420$ so for mobilization and
- NOTE Confidence: 0.805597788571429
- $00:37:33.420 \longrightarrow 00:37:34.984$ biosynthesis of thiol factors.
- NOTE Confidence: 0.805597788571429
- $00:37:34.984 \longrightarrow 00:37:37.156$ So by meaning is that you
- NOTE Confidence: 0.805597788571429
- 00:37:37.156 --> 00:37:39.270 have a different system,
- NOTE Confidence: 0.805597788571429
- $00:37:39.270 \rightarrow 00:37:41.688$ the surfaces here showing in yellow
- NOTE Confidence: 0.805597788571429
- $00:37:41.688 \rightarrow 00:37:44.282$ and perhaps regulating them at a
- NOTE Confidence: 0.805597788571429
- $00:37:44.282 \rightarrow 00:37:46.737$ different conditions can kind of
- NOTE Confidence: 0.805597788571429
- $00{:}37{:}46.737 \dashrightarrow 00{:}37{:}48.824$ regulate specific pathways and
- NOTE Confidence: 0.805597788571429
- $00:37:48.824 \rightarrow 00:37:51.509$ scenario that is completely different.
- NOTE Confidence: 0.805597788571429
- $00{:}37{:}51{.}510 \dashrightarrow 00{:}37{:}53{.}214$ Than organisms that only have one
- NOTE Confidence: 0.805597788571429
- $00:37:53.214 \rightarrow 00:37:54.700$ assisting the self race right?
- NOTE Confidence: 0.805597788571429

00:37:54.700 --> 00:37:58.774 Like you have to have a different.

NOTE Confidence: 0.805597788571429

 $00{:}37{:}58.780 \dashrightarrow 00{:}38{:}00.470$ Mechanism to regulate those different

NOTE Confidence: 0.805597788571429

 $00:38:00.470 \longrightarrow 00:38:00.808$ pathways.

NOTE Confidence: 0.805597788571429

 $00:38:00.810 \longrightarrow 00:38:02.112$ So the experiment that we set

NOTE Confidence: 0.805597788571429

 $00{:}38{:}02{.}112 \dashrightarrow 00{:}38{:}02{.}980$ ourselves to do it,

NOTE Confidence: 0.805597788571429

 $00{:}38{:}02{.}980 \dashrightarrow 00{:}38{:}06{.}655$ it's is if those are so sulfur

NOTE Confidence: 0.805597788571429

00:38:06.655 --> 00:38:07.180 containing

NOTE Confidence: 0.866105306470588

00:38:07.180 --> 00:38:10.288 pathways, do we see a differential

NOTE Confidence: 0.866105306470588

 $00:38:10.288 \longrightarrow 00:38:13.564$ regulation if we grow cells under

NOTE Confidence: 0.866105306470588

 $00:38:13.564 \rightarrow 00:38:16.339$ low sulfur versus high sulfur?

NOTE Confidence: 0.866105306470588

 $00{:}38{:}16{.}340 \dashrightarrow 00{:}38{:}19{.}337$ So what we did here was that we cultured

NOTE Confidence: 0.866105306470588

 $00:38:19.337 \longrightarrow 00:38:22.372$ both type associate solar cells under

NOTE Confidence: 0.866105306470588

 $00{:}38{:}22{.}372 \dashrightarrow 00{:}38{:}24{.}472$ various sulfur concentrations and

NOTE Confidence: 0.866105306470588

 $00:38:24.472 \rightarrow 00:38:27.374$ then we analyze the relative levels

NOTE Confidence: 0.866105306470588

 $00:38:27.374 \rightarrow 00:38:29.977$ of those proteins using Western blot.

NOTE Confidence: 0.866105306470588

 $00:38:29.977 \rightarrow 00:38:32.740$ And So what you can see here is the

- NOTE Confidence: 0.866105306470588
- $00{:}38{:}32{.}820 \dashrightarrow 00{:}38{:}35{.}742$ relative abundance of wire video is
- NOTE Confidence: 0.866105306470588
- $00:38:35.742 \longrightarrow 00:38:38.445$ greatly enhanced under sulfur replete
- NOTE Confidence: 0.866105306470588
- $00:38:38.445 \rightarrow 00:38:43.468$ conditions versus sulfur depleted conditions.
- NOTE Confidence: 0.866105306470588
- $00:38:43.470 \rightarrow 00:38:48.273$ And the same is true for in the MA.
- NOTE Confidence: 0.866105306470588
- $00:38:48.273 \longrightarrow 00:38:50.859$ So what we have observed that
- NOTE Confidence: 0.866105306470588
- 00:38:50.859 00:38:53.309 both components wire VMA,
- NOTE Confidence: 0.866105306470588
- 00:38:53.310 -> 00:38:55.476 they had decrease abundance on on
- NOTE Confidence: 0.866105306470588
- $00{:}38{:}55{.}476 \dashrightarrow 00{:}38{:}56{.}920$ their sulfur limiting condition.
- NOTE Confidence: 0.866105306470588
- 00:38:56.920 --> 00:39:00.286 So if that is the case and then the
- NOTE Confidence: 0.866105306470588
- $00:39:00.286 \rightarrow 00:39:03.642$ other enzymes are not having much
- NOTE Confidence: 0.866105306470588
- $00:39:03.642 \rightarrow 00:39:06.060$ expression what we thought is that
- NOTE Confidence: 0.866105306470588
- $00:39{:}06.060 \dashrightarrow 00{:}39{:}07.900$ under conditions of Christ sulfur
- NOTE Confidence: 0.866105306470588
- $00:39:07.969 \longrightarrow 00:39:10.164$ concentration then this pathway can
- NOTE Confidence: 0.866105306470588
- $00{:}39{:}10.164 \dashrightarrow 00{:}39{:}12.359$ proceed and you get accumulation
- NOTE Confidence: 0.866105306470588
- $00:39:12.428 \longrightarrow 00:39:13.848$ on the fully modified.
- NOTE Confidence: 0.866105306470588

 $00:39:13.850 \longrightarrow 00:39:16.565$ On tyranny and then under

NOTE Confidence: 0.866105306470588

00:39:16.565 --> 00:39:18.194 sulfur depleted conditions,

NOTE Confidence: 0.866105306470588

 $00:39:18.200 \longrightarrow 00:39:20.804$ then you don't get as much

NOTE Confidence: 0.866105306470588

 $00:39:20.804 \rightarrow 00:39:23.020$ as modified to your RNA.

NOTE Confidence: 0.866105306470588

 $00:39:23.020 \longrightarrow 00:39:25.358$ And that's exactly what we have observed.

NOTE Confidence: 0.866105306470588

 $00{:}39{:}25{.}360 \dashrightarrow 00{:}39{:}28{.}360$ So from South culture under different

NOTE Confidence: 0.866105306470588

 $00:39:28.360 \rightarrow 00:39:31.534$ conditions we can analyze the relative

NOTE Confidence: 0.866105306470588

 $00:39:31.534 \rightarrow 00:39:34.254$ levels of those modifications using

NOTE Confidence: 0.866105306470588

 $00{:}39{:}34{.}260 \dashrightarrow 00{:}39{:}37{.}210$ high rates in Ms and we can see a nice

NOTE Confidence: 0.866105306470588

 $00{:}39{:}37{.}289 \dashrightarrow 00{:}39{:}40{.}643$ dose dependent effect on the relative

NOTE Confidence: 0.866105306470588

 $00{:}39{:}40{.}643 \dashrightarrow 00{:}39{:}42{.}879$ accumulation of this modification.

NOTE Confidence: 0.866105306470588

00:39:42.880 --> 00:39:46.592 So put into kind of repeat what I said

NOTE Confidence: 0.866105306470588

 $00:39:46.592 \rightarrow 00:39:49.320$ before is this is an essential pathway,

NOTE Confidence: 0.866105306470588

 $00{:}39{:}49{.}320 \dashrightarrow 00{:}39{:}50{.}828$ an essential modification but

NOTE Confidence: 0.866105306470588

 $00:39:50.828 \rightarrow 00:39:53.090$ you have a cellular contacts that

NOTE Confidence: 0.866105306470588

 $00:39:53.153 \rightarrow 00:39:55.008$ you kind of vary in the degree.

- NOTE Confidence: 0.866105306470588
- 00:39:55.010 --> 00:39:55.982 Of modification,
- NOTE Confidence: 0.866105306470588
- $00:39:55.982 \rightarrow 00:39:58.898$ and presumably you were making the
- NOTE Confidence: 0.866105306470588
- $00:39:58.898 \rightarrow 00:40:01.768$ tyranny less optimal for translation.
- NOTE Confidence: 0.767856469
- $00:40:04.850 \longrightarrow 00:40:07.440$ So what we know also from the
- NOTE Confidence: 0.767856469
- $00{:}40{:}07{.}440 \dashrightarrow 00{:}40{:}09{.}096$ literature that under conditions
- NOTE Confidence: 0.767856469
- $00{:}40{:}09{.}096 \dashrightarrow 00{:}40{:}12{.}393$ that tyranny is hyper modified is not
- NOTE Confidence: 0.767856469
- $00:40:12.393 \rightarrow 00:40:14.923$ fully functional and an offer often
- NOTE Confidence: 0.767856469
- $00{:}40{:}14.923 \dashrightarrow 00{:}40{:}17.185$ hyper modified T RNA's target for
- NOTE Confidence: 0.767856469
- 00:40:17.190 --> 00:40:20.265 degradation and northern blot analysis
- NOTE Confidence: 0.767856469
- $00{:}40{:}20.265 \dashrightarrow 00{:}40{:}24.100$ showed that tyranny that is carried
- NOTE Confidence: 0.767856469
- $00:40:24.100 \longrightarrow 00:40:27.420$ this modification has reduced levels
- NOTE Confidence: 0.767856469
- $00{:}40{:}27.420 \dashrightarrow 00{:}40{:}29.940$ under sulfur depleted accommodations.
- NOTE Confidence: 0.767856469
- 00:40:29.940 --> 00:40:34.105 By analyzing T RNA we can also
- NOTE Confidence: 0.767856469
- $00{:}40{:}34.105 \dashrightarrow 00{:}40{:}36.750$ interrogate the relative levels of
- NOTE Confidence: 0.767856469
- $00:40:36.750 \rightarrow 00:40:39.240$ modifications that depend on this thing.
- NOTE Confidence: 0.767856469

 $00:40:39.240 \longrightarrow 00:40:41.823$ The software is not a wire video

NOTE Confidence: 0.767856469

 $00:40:41.823 \rightarrow 00:40:43.368$ and modifications that presumably

NOTE Confidence: 0.767856469

00:40:43.368 --> 00:40:45.951 depend on on self assess and known

NOTE Confidence: 0.767856469

 $00:40:45.951 \longrightarrow 00:40:48.568$ to depend on ebz two other sustained.

NOTE Confidence: 0.767856469

 $00{:}40{:}48.570 \dashrightarrow 00{:}40{:}50.622$ The software is in this Organism

NOTE Confidence: 0.767856469

 $00:40:50.622 \rightarrow 00:40:52.700$ remain steady under those conditions.

NOTE Confidence: 0.752974525555555

00:40:55.070 --> 00:40:56.835 Yeah, because my lab has

NOTE Confidence: 0.75297452555555

 $00:40:56.835 \longrightarrow 00:40:58.247$ an expertise on iris.

NOTE Confidence: 0.75297452555555

 $00{:}40{:}58.250 \dashrightarrow 00{:}41{:}00.602$ So for Biogenesis we also test the

NOTE Confidence: 0.75297452555555

 $00:41:00.602 \longrightarrow 00:41:02.451$ activity of three different iron

NOTE Confidence: 0.75297452555555

 $00:41:02.451 \longrightarrow 00:41:04.773$ sulfur enzymes to see if those

NOTE Confidence: 0.75297452555555

 $00{:}41{:}04{.}773 \dashrightarrow 00{:}41{:}06.868$ conditions are affecting iron super

NOTE Confidence: 0.75297452555555

 $00:41:06.868 \rightarrow 00:41:09.364$ metabolism and that remains the same.

NOTE Confidence: 0.75297452555555

00:41:09.370 --> 00:41:11.215 Whereas you know likewise enzymes

NOTE Confidence: 0.75297452555555

 $00:41:11.215 \longrightarrow 00:41:13.510$ that do not depend on iris

NOTE Confidence: 0.75297452555555

 $00:41:13.510 \rightarrow 00:41:15.808$ superclusters also is an out there.

- NOTE Confidence: 0.75297452555555
- $00:41:15.810 \longrightarrow 00:41:18.883$ So if it looks like that sulfur
- NOTE Confidence: 0.75297452555555
- $00:41:18.883 \rightarrow 00:41:22.045$ availability has a targeted effect on
- NOTE Confidence: 0.75297452555555
- $00:41:22.045 \rightarrow 00:41:25.555$ modulating the pathway involving wire VO.
- NOTE Confidence: 0.75297452555555
- 00:41:25.560 --> 00:41:29.172 And MDMA and is not really
- NOTE Confidence: 0.75297452555555
- $00:41:29.172 \longrightarrow 00:41:30.978$ disrupting other pathways.
- NOTE Confidence: 0.75297452555555
- $00:41:30.980 \longrightarrow 00:41:32.420$ So, you know,
- NOTE Confidence: 0.75297452555555
- $00:41:32.420 \longrightarrow 00:41:34.820$ in this particular study we
- NOTE Confidence: 0.75297452555555
- $00:41:34.820 \rightarrow 00:41:36.879$ interrogate sulfur availability and
- NOTE Confidence: 0.752974525555555
- $00{:}41{:}36{.}879 \dashrightarrow 00{:}41{:}39{.}909$ then this modification is known to
- NOTE Confidence: 0.75297452555555
- $00:41:39.909 \rightarrow 00:41:42.273$ be affected by other physiological
- NOTE Confidence: 0.75297452555555
- $00:41:42.273 \rightarrow 00:41:46.704$ conditions and we are now carrying on.
- NOTE Confidence: 0.752974525555555
- 00:41:46.710 --> 00:41:47.766 Modification, you know,
- NOTE Confidence: 0.75297452555555
- $00{:}41{:}47.766 \dashrightarrow 00{:}41{:}50.230$ analysis of the relative levels on the
- NOTE Confidence: 0.75297452555555
- $00{:}41{:}50{.}296$ --> $00{:}41{:}52{.}626$ different conditions and testing hypoxia,
- NOTE Confidence: 0.75297452555555
- $00:41:52.630 \longrightarrow 00:41:53.714$ UV radiation,
- NOTE Confidence: 0.75297452555555

 $00:41:53.714 \rightarrow 00:41:56.966$ heat and cold and interrogating the

NOTE Confidence: 0.75297452555555

 $00:41:56.966 \rightarrow 00:41:59.366$ whole effect transcriptome TNA epigen

NOTE Confidence: 0.75297452555555

00:41:59.366 --> 00:42:01.686 script home in Bacillus subtilis.

NOTE Confidence: 0.75297452555555

 $00:42:01.690 \longrightarrow 00:42:04.362$ We do believe that this is not a

NOTE Confidence: 0.75297452555555

 $00:42:04.362 \rightarrow 00:42:06.449$ specific phenomenon to Bacillus subtilis,

NOTE Confidence: 0.75297452555555

 $00{:}42{:}06{.}450 \dashrightarrow 00{:}42{:}08{.}487$ but it's also observed in other types

NOTE Confidence: 0.752974525555555

 $00{:}42{:}08{.}487 \dashrightarrow 00{:}42{:}10{.}260$ of bacteria and we have preliminary

NOTE Confidence: 0.75297452555555

 $00:42:10.260 \rightarrow 00:42:12.610$ data to show that and it's also known,

NOTE Confidence: 0.75297452555555

 $00{:}42{:}12.610 \dashrightarrow 00{:}42{:}16.588$ well documented for different types of.

NOTE Confidence: 0.75297452555555

 $00{:}42{:}16.590 \dashrightarrow 00{:}42{:}18.726$ Product sales and mammals that you

NOTE Confidence: 0.75297452555555

 $00{:}42{:}18.726 \dashrightarrow 00{:}42{:}21.179$ also have some of the equivalent

NOTE Confidence: 0.75297452555555

 $00:42:21.180 \longrightarrow 00:42:22.360$ cellular responses.

NOTE Confidence: 0.8659738805

 $00:42:24.410 \longrightarrow 00:42:26.370$ OK. So the so now it's like

NOTE Confidence: 0.8659738805

 $00:42:26.370 \longrightarrow 00:42:28.512$ the last bit of story that I

NOTE Confidence: 0.8659738805

 $00:42:28.512 \longrightarrow 00:42:30.360$ want to tell you about this,

NOTE Confidence: 0.8659738805

 $00:42:30.360 \longrightarrow 00:42:32.700$ our study on why review MMA.

- NOTE Confidence: 0.8659738805
- $00{:}42{:}32.700 \dashrightarrow 00{:}42{:}35.500$ So we know that those
- NOTE Confidence: 0.8659738805
- 00:42:35.500 00:42:37.740 enzymes are very specific.
- NOTE Confidence: 0.8659738805
- $00:42:37.740 \longrightarrow 00:42:40.105$ The results from the biosynthesis
- NOTE Confidence: 0.8659738805
- $00{:}42{:}40.105 \dashrightarrow 00{:}42{:}42.470$ and also sulfur metabolism project
- NOTE Confidence: 0.8659738805
- $00:42:42.543 \longrightarrow 00:42:44.593$ really informed us that other
- NOTE Confidence: 0.8659738805
- $00{:}42{:}44{.}593 \dashrightarrow 00{:}42{:}47{.}068$ assisting the sulfur races in this
- NOTE Confidence: 0.8659738805
- 00:42:47.068 --> 00:42:49.156 Organism cannot pick up the job
- NOTE Confidence: 0.8659738805
- $00{:}42{:}49.156 \dashrightarrow 00{:}42{:}51.793$ offer wire VO and rescue those
- NOTE Confidence: 0.8659738805
- $00{:}42{:}51{.}793 \dashrightarrow 00{:}42{:}54{.}448$ phenotypes by meaning that wire.
- NOTE Confidence: 0.8659738805
- $00{:}42{:}54{.}450 \dashrightarrow 00{:}42{:}56{.}450$ Video is a dedicated sustained
- NOTE Confidence: 0.8659738805
- $00:42:56.450 \longrightarrow 00:42:59.257$ self race to MMA that plays a
- NOTE Confidence: 0.8659738805
- $00{:}42{:}59{.}257 \dashrightarrow 00{:}43{:}01{.}891$ role once you tie your routine and
- NOTE Confidence: 0.8659738805
- 00:43:01.891 --> 00:43:04.537 you know stuff asked for instance
- NOTE Confidence: 0.8659738805
- $00{:}43{:}04{.}537 \dashrightarrow 00{:}43{:}07{.}768$ cannot be the sulfur source to MMA,
- NOTE Confidence: 0.8659738805
- $00:43:07.770 \longrightarrow 00:43:09.595$ neither all this other system
- NOTE Confidence: 0.8659738805

 $00:43:09.595 \longrightarrow 00:43:10.690$ the soul phrases.

NOTE Confidence: 0.8659738805

 $00:43:10.690 \longrightarrow 00:43:13.672$ We also have in vivo and in

NOTE Confidence: 0.8659738805

 $00:43:13.672 \longrightarrow 00:43:16.518$ vitro data to show that the.

NOTE Confidence: 0.8659738805

 $00:43:16.520 \rightarrow 00:43:18.626$ The dedicated role,

NOTE Confidence: 0.8659738805

 $00{:}43{:}18.626 \dashrightarrow 00{:}43{:}21.756$ it's actually mutual because so

NOTE Confidence: 0.8659738805

 $00{:}43{:}21.756 \dashrightarrow 00{:}43{:}23.652$ few cannot cross react with our

NOTE Confidence: 0.8659738805

 $00:43:23.652 \longrightarrow 00:43:25.778$ view and so on and so forth.

NOTE Confidence: 0.8659738805

 $00:43:25.780 \longrightarrow 00:43:28.706$ So we wanted to understand what are

NOTE Confidence: 0.8659738805

 $00{:}43{:}28.706 \dashrightarrow 00{:}43{:}31.107$ the structure features on those

NOTE Confidence: 0.8659738805

 $00:43:31.107 \rightarrow 00:43:33.777$ enzymes that are really regulating

NOTE Confidence: 0.8659738805

 $00{:}43{:}33{.}777 \dashrightarrow 00{:}43{:}35{.}379$ their physiological functions.

NOTE Confidence: 0.8659738805

 $00:43:35.380 \longrightarrow 00:43:38.138$ So one way to approach that is

NOTE Confidence: 0.8659738805

 $00:43:38.138 \longrightarrow 00:43:40.385$ actually to cost compare the

NOTE Confidence: 0.8659738805

 $00:43:40.385 \rightarrow 00:43:43.300$ closest ortholog to wire view which

NOTE Confidence: 0.8659738805

 $00{:}43{:}43{.}300 \dashrightarrow 00{:}43{:}47{.}016$ is the E coli ISS, so those two.

NOTE Confidence: 0.8659738805

 $00:43:47.016 \longrightarrow 00:43:49.362$ Proteins there are about 63%

- NOTE Confidence: 0.8659738805
- $00{:}43{:}49{.}362 \dashrightarrow 00{:}43{:}51{.}170$ similar to each other,
- NOTE Confidence: 0.8659738805
- $00:43:51.170 \longrightarrow 00:43:53.330$ but yeah they cannot cross
- NOTE Confidence: 0.8659738805
- $00{:}43{:}53{.}330 \dashrightarrow 00{:}43{:}54{.}626$ complement in vivo.
- NOTE Confidence: 0.8659738805
- $00:43:54.630 \rightarrow 00:43:57.566$ So by meaning that if we transform and
- NOTE Confidence: 0.8659738805
- 00:43:57.566 --> 00:44:00.107 express wire view and an E coli cell,
- NOTE Confidence: 0.8659738805
- $00{:}44{:}00{.}110 \dashrightarrow 00{:}44{:}03{.}400$ I cannot rescue the phenotype
- NOTE Confidence: 0.8659738805
- $00:44:03.400 \longrightarrow 00:44:05.374$ associated with ISS.
- NOTE Confidence: 0.8659738805
- $00:44:05.380 \longrightarrow 00:44:07.700$ So this was kind of like part of
- NOTE Confidence: 0.8659738805
- $00{:}44{:}07{.}700 \dashrightarrow 00{:}44{:}10{.}787$ a a initial work where we can
- NOTE Confidence: 0.8659738805
- $00{:}44{:}10.787 \dashrightarrow 00{:}44{:}12.723$ do those cross complementation
- NOTE Confidence: 0.8659738805
- $00:44:12.723 \rightarrow 00:44:14.722$ and expression of wires.
- NOTE Confidence: 0.8659738805
- $00{:}44{:}14.722 \dashrightarrow 00{:}44{:}17.014$ The old the vessel assisting the
- NOTE Confidence: 0.8659738805
- 00:44:17.014 --> 00:44:18.908 sofras cannot react cross react
- NOTE Confidence: 0.8659738805
- 00:44:18.908 --> 00:44:21.274 with us A and rescue their pathway.
- NOTE Confidence: 0.8659738805
- $00{:}44{:}21{.}280 \dashrightarrow 00{:}44{:}23{.}961$ But if we Co express both vessels
- NOTE Confidence: 0.8659738805

- 00:44:23.961 --> 00:44:27.299 operating in an ISS knockout of equal life,
- NOTE Confidence: 0.8659738805
- $00{:}44{:}27{.}300 \dashrightarrow 00{:}44{:}29{.}252$ we can fully rescue.
- NOTE Confidence: 0.8659738805
- $00{:}44{:}29{.}252 \dashrightarrow 00{:}44{:}33{.}299$ The same is true for admission in the MA.
- NOTE Confidence: 0.8659738805
- 00:44:33.299 00:44:35.910 We can only rescue if we express.
- NOTE Confidence: 0.8659738805
- $00{:}44{:}35{.}910 \dashrightarrow 00{:}44{:}38{.}560$ This pathway.
- NOTE Confidence: 0.8659738805
- $00:44:38.560 \rightarrow 00:44:40.036$ At the same time,
- NOTE Confidence: 0.8659738805
- $00:44:40.036 \longrightarrow 00:44:42.837$ so that tells us there's a specific
- NOTE Confidence: 0.8659738805
- 00:44:42.837 --> 00:44:46.358 sulfur transfer from wire video to MMA,
- NOTE Confidence: 0.8659738805
- $00{:}44{:}46{.}360 \dashrightarrow 00{:}44{:}49{.}000$ and that sulfur transfer event
- NOTE Confidence: 0.8659738805
- $00{:}44{:}49{.}000 \dashrightarrow 00{:}44{:}51{.}659$ cannot happen as prevented somehow
- NOTE Confidence: 0.8659738805
- $00:44:51.659 \longrightarrow 00:44:54.324$ from wire reveal to Tuesday
- NOTE Confidence: 0.8659738805
- $00:44:54.324 \longrightarrow 00:44:57.229$ to rescue that ecoli pathway.
- NOTE Confidence: 0.8659738805
- $00{:}44{:}57{.}230 \dashrightarrow 00{:}45{:}00{.}022$ So that kind of provide the premise for
- NOTE Confidence: 0.8659738805
- $00:45:00.022 \rightarrow 00:45:02.197$ a series of biochemical experiments
- NOTE Confidence: 0.8659738805
- 00:45:02.197 -> 00:45:04.993 where we test the cross reactivity
- NOTE Confidence: 0.8659738805
- $00:45:04.993 \longrightarrow 00:45:07.788$ of those enzymes in the test tube.

- NOTE Confidence: 0.8659738805
- $00:45:07.790 \rightarrow 00:45:11.465$ So again via video enhances the catalytic
- NOTE Confidence: 0.8659738805
- 00:45:11.465 --> 00:45:15.169 activity of its physiological partner,
- NOTE Confidence: 0.8659738805
- $00{:}45{:}15{.}170 \dashrightarrow 00{:}45{:}18{.}362$ but it does not react with the ecoli
- NOTE Confidence: 0.8659738805
- $00:45:18.362 \rightarrow 00:45:21.038$ ortholog and then the ecoli system.
- NOTE Confidence: 0.8659738805
- $00:45:21.040 \longrightarrow 00:45:23.224$ The suffrage can only have its
- NOTE Confidence: 0.8659738805
- $00{:}45{:}23.224 \dashrightarrow 00{:}45{:}24.680$ activity enhanced in presence
- NOTE Confidence: 0.8659738805
- $00:45:24.749 \rightarrow 00:45:26.329$ of its geological partner,
- NOTE Confidence: 0.8659738805
- $00:45:26.330 \longrightarrow 00:45:27.033$ the.
- NOTE Confidence: 0.8659738805
- $00{:}45{:}27.033 \dashrightarrow 00{:}45{:}30.548$ Why are video doesn't display
- NOTE Confidence: 0.8659738805
- $00:45:30.550 \longrightarrow 00:45:31.873$ that phenomenon so?
- NOTE Confidence: 0.8659738805
- $00:45:31.873 \rightarrow 00:45:34.519$ We know those enzymes are catalyzing
- NOTE Confidence: 0.8659738805
- $00{:}45{:}34{.}519$ --> $00{:}45{:}36{.}446$ the same chemical reaction
- NOTE Confidence: 0.8659738805
- $00:45:36.446 \longrightarrow 00:45:38.796$ which is sulfur transfer from
- NOTE Confidence: 0.8659738805
- $00:45:38.796 \longrightarrow 00:45:41.139$ cysteine to a sulfur receptor.
- NOTE Confidence: 0.8659738805
- $00:45:41.140 \longrightarrow 00:45:44.213$ And then we took advantage of a
- NOTE Confidence: 0.8659738805

00:45:44.213 --> 00:45:46.456 crystal structure that was available

NOTE Confidence: 0.8659738805

 $00{:}45{:}46{.}456 \dashrightarrow 00{:}45{:}49{.}410$ in of ecoli ICS in complex where

NOTE Confidence: 0.8659738805

 $00{:}45{:}49{.}410 \dashrightarrow 00{:}45{:}52{.}111$ Texas A and we match the residues NOTE Confidence: 0.8659738805

 $00:45:52.111 \rightarrow 00:45:56.090$ that were at this binding interface.

NOTE Confidence: 0.8659738805

 $00{:}45{:}56{.}090 \dashrightarrow 00{:}45{:}58{.}555$ And we postulated that perhaps

NOTE Confidence: 0.8659738805

 $00:45:58.555 \longrightarrow 00:46:01.528$ the lack of cross reactivity of

NOTE Confidence: 0.8659738805

 $00{:}46{:}01{.}528 \dashrightarrow 00{:}46{:}03{.}618$ the Bacillus assisting the sulfur

NOTE Confidence: 0.8659738805

 $00{:}46{:}03.618 \dashrightarrow 00{:}46{:}06.672$ ace in E coli was associated with

NOTE Confidence: 0.8659738805

 $00{:}46{:}06{.}672 \dashrightarrow 00{:}46{:}07{.}968$ a now third

NOTE Confidence: 0.67446936

 $00:46:07.970 \longrightarrow 00:46:11.160$ binding interface.

NOTE Confidence: 0.67446936

 $00{:}46{:}11{.}160 \dashrightarrow 00{:}46{:}13{.}128$ So what we did here is

NOTE Confidence: 0.67446936

 $00:46:13.128 \longrightarrow 00:46:14.440$ to guide those analysis.

NOTE Confidence: 0.67446936

 $00{:}46{:}14{.}440 \dashrightarrow 00{:}46{:}17{.}040$ We conducted a multi sequence

NOTE Confidence: 0.67446936

 $00{:}46{:}17.040 \dashrightarrow 00{:}46{:}20.040$ alignment using several sequences of ice.

NOTE Confidence: 0.67446936

 $00:46:20.040 \longrightarrow 00:46:21.475$ So this is just an example here.

NOTE Confidence: 0.67446936

 $00:46:21.480 \rightarrow 00:46:23.765$ But several sequences of organisms

 $00:46:23.765 \rightarrow 00:46:26.494$ that contain ISS like enzymes and

NOTE Confidence: 0.67446936

 $00{:}46{:}26{.}494 \dashrightarrow 00{:}46{:}29{.}091$ use staff as partners and in several

NOTE Confidence: 0.67446936

 $00{:}46{:}29.091 \dashrightarrow 00{:}46{:}31.337$ organs that contain wire veal like

NOTE Confidence: 0.67446936

00:46:31.337 --> 00:46:33.851 enzymes and use and then MA as

NOTE Confidence: 0.67446936

 $00{:}46{:}33{.}851 \dashrightarrow 00{:}46{:}35{.}706$ sort of an abbreviated pathway.

NOTE Confidence: 0.67446936

 $00{:}46{:}35{.}710 \dashrightarrow 00{:}46{:}37{.}718$ And then we try to map residues that

NOTE Confidence: 0.67446936

 $00{:}46{:}37.718 \dashrightarrow 00{:}46{:}39.579$ were shared within those groups but

NOTE Confidence: 0.67446936

 $00:46:39.579 \longrightarrow 00:46:41.529$ there were distinct between those two.

NOTE Confidence: 0.67446936

 $00{:}46{:}41.530 \dashrightarrow 00{:}46{:}44.050$ Families of assisting the cell for assist.

NOTE Confidence: 0.67446936

 $00:46:44.050 \longrightarrow 00:46:46.450$ So although they have a high

NOTE Confidence: 0.67446936

 $00:46:46.450 \longrightarrow 00:46:47.650$ degree of similarity,

NOTE Confidence: 0.67446936

 $00{:}46{:}47.650 \dashrightarrow 00{:}46{:}50.080$ there were some key differences in.

NOTE Confidence: 0.67446936

 $00:46:50.080 \longrightarrow 00:46:52.328$ I want to point here on this table.

NOTE Confidence: 0.67446936

 $00:46:52.330 \longrightarrow 00:46:56.187$ So what do you see is that?

NOTE Confidence: 0.67446936

 $00:46:56.190 \rightarrow 00:46:58.060$ And it's very interesting is

 $00:46:58.060 \longrightarrow 00:47:00.282$ that some of the residues that

NOTE Confidence: 0.67446936

 $00:47:00.282 \longrightarrow 00:47:02.908$ are at the binding interface,

NOTE Confidence: 0.67446936

 $00{:}47{:}02{.}908 \dashrightarrow 00{:}47{:}06{.}973$ we thus say for instance glutamate 48 NOTE Confidence: 0.67446936

 $00:47:06.973 \rightarrow 00:47:10.053$ and 49 in ecoli had opposite charge

NOTE Confidence: 0.67446936

 $00{:}47{:}10.053 \dashrightarrow 00{:}47{:}13.778$ in the wire video sequence and that

NOTE Confidence: 0.67446936

 $00{:}47{:}13.780 \dashrightarrow 00{:}47{:}16.402$ provide the basis for a proposal

NOTE Confidence: 0.67446936

 $00{:}47{:}16{.}402 \dashrightarrow 00{:}47{:}19{.}200$ that those proteins were not cross

NOTE Confidence: 0.67446936

 $00:47:19.200 \rightarrow 00:47:22.098$ reacting because they were not having

NOTE Confidence: 0.67446936

 $00{:}47{:}22.098 \dashrightarrow 00{:}47{:}25.336$ a complementary charge afforded by that.

NOTE Confidence: 0.67446936

 $00{:}47{:}25{.}336 \dashrightarrow 00{:}47{:}25{.}854$ Surface.

NOTE Confidence: 0.67446936

 $00{:}47{:}25.854 \dashrightarrow 00{:}47{:}29.480$ Also important to note here is that

NOTE Confidence: 0.67446936

 $00:47:29.577 \longrightarrow 00:47:33.002$ this binding interface between

NOTE Confidence: 0.67446936

 $00:47:33.002 \rightarrow 00:47:37.656$ ISIS and Tus 8/6 as I remote.

NOTE Confidence: 0.67446936

 $00{:}47{:}37.656 \dashrightarrow 00{:}47{:}40.349$ So the active site is here and you

NOTE Confidence: 0.67446936

 $00{:}47{:}40{.}349 \dashrightarrow 00{:}47{:}42{.}792$ have a loop that swings into the

NOTE Confidence: 0.67446936

 $00{:}47{:}42.792 \dashrightarrow 00{:}47{:}45.299$ active side and donates the sulfur.

- NOTE Confidence: 0.67446936
- $00:47:45.300 \longrightarrow 00:47:47.295$ So the binding interface between
- NOTE Confidence: 0.67446936
- $00{:}47{:}47{.}295 \dashrightarrow 00{:}47{:}49{.}759$ the enzyme and the sulfur receptor
- NOTE Confidence: 0.67446936
- $00:47:49.759 \rightarrow 00:47:52.153$ occurs at remote site and actually
- NOTE Confidence: 0.67446936
- $00{:}47{:}52{.}153 \dashrightarrow 00{:}47{:}54{.}656$ at a different sub unit where
- NOTE Confidence: 0.67446936
- $00:47:54.656 \longrightarrow 00:47:56.304$ the catalytic chemistry is.
- NOTE Confidence: 0.67446936
- 00:47:56.310 --> 00:47:57.540 Company,
- NOTE Confidence: 0.67446936
- 00:47:57.540 --> 00:47:58.770 OK.
- NOTE Confidence: 0.67446936
- $00:47:58.770 \longrightarrow 00:48:00.630$ So the obviously experiment that
- NOTE Confidence: 0.67446936
- $00{:}48{:}00{.}630 \dashrightarrow 00{:}48{:}03{.}618$ we set up ourselves to do is like
- NOTE Confidence: 0.67446936
- 00:48:03.618 --> 00:48:05.730 construct a library of mutants and
- NOTE Confidence: 0.67446936
- $00{:}48{:}05{.}730 \dashrightarrow 00{:}48{:}08{.}350$ trying to take wire video and convert
- NOTE Confidence: 0.67446936
- $00{:}48{:}08{.}350 \dashrightarrow 00{:}48{:}11{.}290$ into ISS like by modifying those
- NOTE Confidence: 0.67446936
- $00:48:11.290 \longrightarrow 00:48:13.533$ select residues into residues that
- NOTE Confidence: 0.67446936
- 00:48:13.533 --> 00:48:16.861 are present in ISS and see if we
- NOTE Confidence: 0.67446936
- $00{:}48{:}16.861 \dashrightarrow 00{:}48{:}19.849$ can expand the reactivity of this NOTE Confidence: 0.67446936
$00:48:19.849 \rightarrow 00:48:23.939$ enzyme towards equalized so for acceptors.

NOTE Confidence: 0.67446936

 $00{:}48{:}23{.}940 \dashrightarrow 00{:}48{:}26{.}424$ So we first passed the reactivity

NOTE Confidence: 0.67446936

 $00{:}48{:}26{.}424 \dashrightarrow 00{:}48{:}28{.}482$ towards the native effectors and

NOTE Confidence: 0.67446936

 $00{:}48{:}28{.}482 \dashrightarrow 00{:}48{:}30{.}486$ you know some of those residues

NOTE Confidence: 0.67446936

 $00{:}48{:}30{.}486 \dashrightarrow 00{:}48{:}32{.}940$ here they lost the ability to

NOTE Confidence: 0.67446936

 $00:48:32.940 \longrightarrow 00:48:35.060$ engage with the native acceptor,

NOTE Confidence: 0.67446936

 $00:48:35.060 \longrightarrow 00:48:37.910$ but most importantly.

NOTE Confidence: 0.67446936

00:48:37.910 --> 00:48:40.826 By doing this music Genesis studies

NOTE Confidence: 0.67446936

 $00{:}48{:}40.826 \dashrightarrow 00{:}48{:}44.468$ we could screen that some of

NOTE Confidence: 0.67446936

 $00:48:44.468 \rightarrow 00:48:49.203$ those mutations so 44, so R44E.

NOTE Confidence: 0.67446936

 $00:48:49.203 \rightarrow 00:48:51.756$ Why are VOC?

NOTE Confidence: 0.67446936

 $00:48:51.760 \rightarrow 00:48:54.238$ The head contain equivalent mutation here.

NOTE Confidence: 0.67446936

 $00{:}48{:}54{.}240 \dashrightarrow 00{:}48{:}59{.}200$ So when we mutated to look like ISS

NOTE Confidence: 0.67446936

 $00:48:59.200 \longrightarrow 00:49:03.640$ now we can engage in a reaction with

NOTE Confidence: 0.67446936

 $00:49:03.640 \longrightarrow 00:49:06.240$ pasta and have these activities

NOTE Confidence: 0.67446936

00:49:06.336 --> 00:49:09.732 stimulation to you know over tenfold

 $00:49:09.732 \longrightarrow 00:49:13.130$ on the catalytic turnover rate and

NOTE Confidence: 0.67446936

 $00{:}49{:}13.130 \dashrightarrow 00{:}49{:}15.735$ this is another super receptor.

NOTE Confidence: 0.67446936

 $00:49:15.740 \longrightarrow 00:49:18.071$ I that we don't have a crystal

NOTE Confidence: 0.67446936

 $00:49:18.071 \rightarrow 00:49:19.700$ structure for the complex,

NOTE Confidence: 0.67446936

 $00{:}49{:}19{.}700 \dashrightarrow 00{:}49{:}22{.}353$ but when we mutate 4 residues at

NOTE Confidence: 0.67446936

 $00:49:22.353 \rightarrow 00:49:24.240$ that particular binding interface,

NOTE Confidence: 0.67446936

 $00:49:24.240 \rightarrow 00:49:27.810$ we observe a high degree of extenuation,

NOTE Confidence: 0.67446936

 $00:49:27.810 \longrightarrow 00:49:31.835$ so suggesting that we are kind of.

NOTE Confidence: 0.67446936

 $00{:}49{:}31.840 \dashrightarrow 00{:}49{:}33.616$ Who were somewhat successful

NOTE Confidence: 0.67446936

 $00:49:33.616 \longrightarrow 00:49:35.836$ in engineering those enzymes to

NOTE Confidence: 0.67446936

00:49:35.836 --> 00:49:39.036 now adopt in a very intentional

NOTE Confidence: 0.67446936

 $00:49:39.036 \rightarrow 00:49:41.684$ mariner expanded reactivity towards

NOTE Confidence: 0.67446936

 $00:49:41.684 \rightarrow 00:49:43.060$ selected pathways.

NOTE Confidence: 0.67446936

 $00{:}49{:}43.060 \dashrightarrow 00{:}49{:}46.616$ So to validate some of those findings,

NOTE Confidence: 0.67446936

 $00:49:46.620 \longrightarrow 00:49:50.316$ what we did here is that we.

 $00{:}49{:}50{.}320 \dashrightarrow 00{:}49{:}54{.}296$ We wanted to determine whether or not

NOTE Confidence: 0.67446936

 $00:49:54.296 \rightarrow 00:49:57.815$ those variant enzymes were able to

NOTE Confidence: 0.67446936

 $00{:}49{:}57{.}815 \dashrightarrow 00{:}50{:}01{.}689$ partake role on ISS pathways in vivo.

NOTE Confidence: 0.67446936

 $00:50:01.690 \dashrightarrow 00:50:05.980$ So to do that work we use a ISS knockout

NOTE Confidence: 0.8321999435

 $00:50:06.090 \dashrightarrow 00:50:09.438$ strain and we know that this

NOTE Confidence: 0.8321999435

 $00:50:09.438 \longrightarrow 00:50:12.454$ is spraying is affected in its

NOTE Confidence: 0.8321999435

 $00:50:12.454 \rightarrow 00:50:14.806$ ability to make four thought errity

NOTE Confidence: 0.8321999435

 $00:50:14.806 \rightarrow 00:50:17.849$ in a pathway that depends on ,

NOTE Confidence: 0.8321999435

 $00{:}50{:}17.850 \dashrightarrow 00{:}50{:}20.755$ and it's also affected in a pathway.

NOTE Confidence: 0.8321999435

 $00:50:20.760 \longrightarrow 00:50:24.310$ To make 2 thyroxine in a through

NOTE Confidence: 0.8321999435

 $00{:}50{:}24.310 \dashrightarrow 00{:}50{:}27.310$ through engagement with us a.

NOTE Confidence: 0.8321999435

 $00:50:27.310 \longrightarrow 00:50:29.320$ When we express the wall

NOTE Confidence: 0.8321999435

00:50:29.320 --> 00:50:30.928 type of stimulus enzyme,

NOTE Confidence: 0.8321999435

 $00:50:30.930 \rightarrow 00:50:33.366$ we don't really rescue those pathways,

NOTE Confidence: 0.8321999435

 $00{:}50{:}33{.}370 \dashrightarrow 00{:}50{:}35{.}716$ so this is relative levels to

NOTE Confidence: 0.8321999435

 $00:50:35.716 \rightarrow 00:50:37.870$ the wall type equalized strain.

- NOTE Confidence: 0.8321999435
- $00{:}50{:}37{.}870 \dashrightarrow 00{:}50{:}40{.}235$ However, when we take the
- NOTE Confidence: 0.8321999435
- 00:50:40.235 --> 00:50:43.840 single point mutation R44E,
- NOTE Confidence: 0.8321999435
- $00:50:43.840 \longrightarrow 00:50:47.130$ what we're able to achieve is fully
- NOTE Confidence: 0.8321999435
- $00:50:47.130 \rightarrow 00:50:49.761$ recovery of two pyridine pathway
- NOTE Confidence: 0.8321999435
- $00:50:49.761 \rightarrow 00:50:53.485$ indicating that it took only one single
- NOTE Confidence: 0.8321999435
- $00{:}50{:}53{.}582 \dashrightarrow 00{:}50{:}57{.}397$ amino acid substitution to convert via VOA.
- NOTE Confidence: 0.8321999435
- $00:50:57.400 \rightarrow 00:51:01.568$ Into an ISS like enzyme in the pathway
- NOTE Confidence: 0.8321999435
- $00:51:01.568 \rightarrow 00:51:03.430$ requiring to say those results are
- NOTE Confidence: 0.8321999435
- $00:51:03.430 \rightarrow 00:51:05.419$ kind of in agreement with the system,
- NOTE Confidence: 0.8321999435
- $00{:}51{:}05{.}420 \dashrightarrow 00{:}51{:}07{.}625$ the self race because that's the mutant
- NOTE Confidence: 0.8321999435
- $00:51:07.625 \rightarrow 00:51:10.178$ that we could show activity stimulation.
- NOTE Confidence: 0.8321999435
- $00:51:10.180 \rightarrow 00:51:12.955$ Likewise this wire deal quadruple
- NOTE Confidence: 0.8321999435
- $00:51:12.955 \rightarrow 00:51:16.074$ mutant here could engage with I,
- NOTE Confidence: 0.8321999435
- $00{:}51{:}16.074 \dashrightarrow 00{:}51{:}19.203$ I and recovery if not even more
- NOTE Confidence: 0.8321999435
- 00:51:19.203 --> 00:51:20.939 accumulation of 4th iritty.
- NOTE Confidence: 0.8321999435

 $00:51:20.940 \rightarrow 00:51:23.940$ And that's a pathway that depends on thi.

NOTE Confidence: 0.8321999435

00:51:23.940 --> 00:51:25.970 This mutant again was a mutant that

NOTE Confidence: 0.8321999435

 $00{:}51{:}25{.}970 \dashrightarrow 00{:}51{:}28{.}519$ showed a 20 fold activity stimulation.

NOTE Confidence: 0.8321999435

 $00{:}51{:}28{.}520 \dashrightarrow 00{:}51{:}32{.}838$ So we're really pleased with this and

NOTE Confidence: 0.8321999435

 $00{:}51{:}32.838 \dashrightarrow 00{:}51{:}35.688$ kind of struck by the results that

NOTE Confidence: 0.8321999435

00:51:35.688 --> 00:51:38.397 you know it takes only one change

NOTE Confidence: 0.8321999435

00:51:38.480 --> 00:51:40.958 for for a gain of functionality.

NOTE Confidence: 0.8321999435

 $00{:}51{:}40{.}960 \dashrightarrow 00{:}51{:}45{.}060$ We also look at in terms of

NOTE Confidence: 0.8321999435

 $00{:}51{:}45{.}060 \dashrightarrow 00{:}51{:}45{.}740$ growth phenotypes.

NOTE Confidence: 0.8321999435

 $00:51:45.740 \longrightarrow 00:51:49.142$ So ISS is involved with so

NOTE Confidence: 0.8321999435

 $00:51:49.142 \longrightarrow 00:51:50.843$ many cellular processes.

NOTE Confidence: 0.8321999435

 $00{:}51{:}50{.}850 \dashrightarrow 00{:}51{:}53{.}518$ Inactivation of ISS causes

NOTE Confidence: 0.8321999435

 $00:51:53.518 \rightarrow 00:51:56.186$ a severe growth phenotype.

NOTE Confidence: 0.8321999435

 $00:51:56.190 \rightarrow 00:51:57.990$ If we express the wall type,

NOTE Confidence: 0.8321999435

00:51:57.990 --> 00:51:59.538 it doesn't really help,

NOTE Confidence: 0.8321999435

 $00:51:59.538 \rightarrow 00:52:01.086$ it actually makes worse.

- NOTE Confidence: 0.8321999435
- $00{:}52{:}01.090 \dashrightarrow 00{:}52{:}04.360$ But expression of that single
- NOTE Confidence: 0.8321999435
- $00:52:04.360 \longrightarrow 00:52:06.976$ mutant partially recovers ISS.
- NOTE Confidence: 0.8321999435
- $00:52:06.980 \longrightarrow 00:52:09.055$ We didn't observe full recovery
- NOTE Confidence: 0.8321999435
- $00:52:09.055 \longrightarrow 00:52:12.323$ in relation to the wild type and
- NOTE Confidence: 0.8321999435
- $00:52:12.323 \rightarrow 00:52:14.555$ that's actually expected because
- NOTE Confidence: 0.8321999435
- $00{:}52{:}14.555 \dashrightarrow 00{:}52{:}17.245$ we're selectively recovering one of
- NOTE Confidence: 0.8321999435
- $00:52:17.245 \rightarrow 00:52:19.446$ the pathways that ICS participate.
- NOTE Confidence: 0.8321999435
- $00:52:19.446 \rightarrow 00:52:22.920$ So in the end, you know my background,
- NOTE Confidence: 0.8321999435
- $00:52:22.920 \rightarrow 00:52:24.460$ other pathways involving ISS,
- NOTE Confidence: 0.8321999435
- $00:52:24.460 \longrightarrow 00:52:27.780$ they still depleted and contributing
- NOTE Confidence: 0.8321999435
- $00:52:27.780 \longrightarrow 00:52:29.344$ to growth,
- NOTE Confidence: 0.8321999435
- $00{:}52{:}29{.}344 \dashrightarrow 00{:}52{:}34.036$ growth rates in this particular Organism.
- NOTE Confidence: 0.8321999435
- $00:52:34.040 \longrightarrow 00:52:34.382$ OK.
- NOTE Confidence: 0.8321999435
- $00{:}52{:}34{.}382 \dashrightarrow 00{:}52{:}35{.}408$ So with that,
- NOTE Confidence: 0.8321999435
- $00{:}52{:}35{.}408 \dashrightarrow 00{:}52{:}38{.}320$ I don't know how I'm doing with time,
- NOTE Confidence: 0.8321999435

 $00{:}52{:}38{.}320 \dashrightarrow 00{:}52{:}40{.}952$ but the main take away points that

NOTE Confidence: 0.8321999435

 $00:52:40.952 \longrightarrow 00:52:43.758$ I want you to kind of remember

NOTE Confidence: 0.8321999435

00:52:43.760 --> 00:52:46.736 from from this talk is that T RNA

NOTE Confidence: 0.8321999435

 $00:52:46.736 \longrightarrow 00:52:48.539$ performs multiple roles besides

NOTE Confidence: 0.8321999435

 $00{:}52{:}48{.}539 \dashrightarrow 00{:}52{:}51{.}473$ translation and those roles are really

NOTE Confidence: 0.8321999435

 $00{:}52{:}51{.}473 \dashrightarrow 00{:}52{:}53{.}920$ important that defects on enzymes, NOTE Confidence: 0.8321999435

 $00{:}52{:}53{.}920 \dashrightarrow 00{:}52{:}56{.}335$ they modify T RNA and like some

NOTE Confidence: 0.8321999435

 $00:52:56.335 \longrightarrow 00:52:58.729$ some folks in the field they

NOTE Confidence: 0.8321999435

 $00:52:58.729 \longrightarrow 00:53:00.437$ call riders TNA writers,

NOTE Confidence: 0.8321999435

 $00{:}53{:}00{.}440 \dashrightarrow 00{:}53{:}02{.}840$ they are associated with multiple

NOTE Confidence: 0.8321999435

 $00{:}53{:}02{.}840 \dashrightarrow 00{:}53{:}04{.}760$ pathologies and cellular viability.

NOTE Confidence: 0.8321999435

 $00:53:04.760 \longrightarrow 00:53:07.270$ That the abundance of those

NOTE Confidence: 0.8321999435

 $00:53:07.270 \longrightarrow 00:53:09.278$ modifications are impacted by

NOTE Confidence: 0.8321999435

 $00:53:09.280 \longrightarrow 00:53:10.716$ nutrient availability and then

NOTE Confidence: 0.8321999435

00:53:10.716 --> 00:53:12.870 I showed you the example about

NOTE Confidence: 0.8321999435

 $00:53:12.930 \longrightarrow 00:53:15.210$ sulfur concentration but also their

 $00:53:15.210 \longrightarrow 00:53:17.110$ environmental factors that fine-tuned

NOTE Confidence: 0.8321999435

 $00:53:17.110 \longrightarrow 00:53:19.760$ the functionality of transfer RNA.

NOTE Confidence: 0.8321999435

 $00:53:19.760 \longrightarrow 00:53:22.440$ Then in Bacillus subtilis at

NOTE Confidence: 0.8321999435

 $00:53:22.440 \longrightarrow 00:53:24.711$ least those modifications they

NOTE Confidence: 0.8321999435

 $00:53:24.711 \rightarrow 00:53:27.596$ involve dedicated enzymes and the

NOTE Confidence: 0.8321999435

 $00{:}53{:}27{.}596 \dashrightarrow 00{:}53{:}29{.}790$ interaction between the assisting

NOTE Confidence: 0.8321999435

 $00:53:29.790 \rightarrow 00:53:32.676$ the surprises and they are sulfur

NOTE Confidence: 0.8321999435

 $00:53:32.676 \rightarrow 00:53:35.118$ receptor partners is a very specific.

NOTE Confidence: 0.8321999435

 $00:53:35.120 \longrightarrow 00:53:38.726$ Event that directs sulfur to the

NOTE Confidence: 0.8321999435

 $00:53:38.726 \rightarrow 00:53:40.529$ pathways they're participating.

NOTE Confidence: 0.8321999435

 $00:53:40.530 \longrightarrow 00:53:41.850$ And then with that,

NOTE Confidence: 0.8321999435

 $00{:}53{:}41{.}850 \dashrightarrow 00{:}53{:}44{.}594$ I want to thank the people that have

NOTE Confidence: 0.8321999435

 $00:53:44.594 \rightarrow 00:53:47.610$ done the work. I have a very young lab.

NOTE Confidence: 0.8321999435

 $00{:}53{:}47.610 \dashrightarrow 00{:}53{:}50.368$ You may recognize the last name here.

NOTE Confidence: 0.8321999435

00:53:50.370 --> 00:53:53.910 So nick?

 $00:53:53.910 \rightarrow 00:53:55.902$ It was a member of my lab, he graduated.

NOTE Confidence: 0.8321999435

 $00{:}53{:}55{.}902 \dashrightarrow 00{:}53{:}58{.}830$ But I I'm very thankful for all the

NOTE Confidence: 0.809717455833333

 $00:53:58.904 \longrightarrow 00:54:01.156$ students that, graduate and

NOTE Confidence: 0.809717455833333

 $00:54:01.156 \dashrightarrow 00:54:03.568$ undergraduate students that and

NOTE Confidence: 0.809717455833333

 $00:54:03.570 \longrightarrow 00:54:05.726$ are in the lab doing hard work,

NOTE Confidence: 0.809717455833333

 $00{:}54{:}05{.}730 \dashrightarrow 00{:}54{:}08{.}530$ and also my collaborators that.

NOTE Confidence: 0.909748937142857

 $00:54:10.870 \rightarrow 00:54:12.724$ Very important for other projects that

NOTE Confidence: 0.909748937142857

 $00:54:12.724 \rightarrow 00:54:14.909$ I have not talked to you about it.

NOTE Confidence: 0.909748937142857

 $00{:}54{:}14{.}910 \dashrightarrow 00{:}54{:}17{.}460$ I'm also thankful for the National

NOTE Confidence: 0.909748937142857

 $00{:}54{:}17{.}460 \dashrightarrow 00{:}54{:}20{.}020$ Science Foundation that has been mainly

NOTE Confidence: 0.909748937142857

 $00{:}54{:}20{.}020 \dashrightarrow 00{:}54{:}22{.}134$ funded this this project and other

NOTE Confidence: 0.909748937142857

00:54:22.134 --> 00:54:24.630 projects in my lab since they started

NOTE Confidence: 0.909748937142857

 $00{:}54{:}24{.}630 \dashrightarrow 00{:}54{:}26{.}310$ and then thank you for your attention.

NOTE Confidence: 0.38838714

 $00{:}54{:}31{.}300 \dashrightarrow 00{:}54{:}32{.}530$ It's time for a public question.

NOTE Confidence: 0.4727253

 $00{:}54{:}36{.}090 \dashrightarrow 00{:}54{:}36{.}840$ Chat.

NOTE Confidence: 0.8725853

 $00{:}54{:}42{.}420 \dashrightarrow 00{:}54{:}43{.}150$ Yeah.

- NOTE Confidence: 0.733557336
- $00{:}54{:}47{.}340 \dashrightarrow 00{:}54{:}50{.}010$ Oh, I'm sorry. So so

 $00:54:50.960 \dashrightarrow 00:54:55.505$ how do I close? You know the first point.

NOTE Confidence: 0.7732843

 $00{:}54{:}55{.}505 \dashrightarrow 00{:}54{:}56{.}772$ The modification was carried

NOTE Confidence: 0.7732843

 $00:54:56.772 \longrightarrow 00:54:58.340$ in the non canonical function.

NOTE Confidence: 0.1721715

 $00{:}55{:}00{.}760 \dashrightarrow 00{:}55{:}01{.}430$ Umm.

NOTE Confidence: 0.692440166

 $00{:}55{:}04{.}110 \dashrightarrow 00{:}55{:}09{.}008$ OK. So let's do that. Uh.

NOTE Confidence: 0.692440166

00:55:09.008 --> 00:55:11.150 There we go. OK. Sorry.

NOTE Confidence: 0.07768679

 $00:55:13.890 \longrightarrow 00:55:14.480$ Curated.

NOTE Confidence: 0.47206411

 $00{:}55{:}17.250 \dashrightarrow 00{:}55{:}20.860$ Partner talk. Are the modifications to the

NOTE Confidence: 0.47206411

 $00:55:20.860 \longrightarrow 00:55:23.345$ modifications of the tyranny that dictate the

NOTE Confidence: 0.660914215714286

 $00:55:23.360 \rightarrow 00:55:25.824$ other the other problems like in viral?

NOTE Confidence: 0.6988261

 $00{:}55{:}27{.}540 \dashrightarrow 00{:}55{:}32{.}430$ Yeah. Directs the.

NOTE Confidence: 0.6988261

 $00{:}55{:}32{.}430 \dashrightarrow 00{:}55{:}34{.}817$ So you know that's a really great

NOTE Confidence: 0.6988261

 $00:55:34.817 \dashrightarrow 00:55:36.732$ one because for example tyranny

NOTE Confidence: 0.6988261

 $00{:}55{:}36{.}732 \dashrightarrow 00{:}55{:}39{.}192$ lysine and it's modified form is

 $00:55:39.192 \rightarrow 00:55:41.970$ actually a primer for HIV replication.

NOTE Confidence: 0.6988261

 $00:55:41.970 \rightarrow 00:55:45.048$ So that modification is really important.

NOTE Confidence: 0.6988261

 $00{:}55{:}45{.}050 \dashrightarrow 00{:}55{:}47{.}586$ I think the work that I just showed

NOTE Confidence: 0.6988261

 $00{:}55{:}47{.}586 \dashrightarrow 00{:}55{:}49{.}814$ you in its modified form and then the

NOTE Confidence: 0.6988261

 $00{:}55{:}49{.}814 \dashrightarrow 00{:}55{:}51{.}994$ work that I kind of show you here

NOTE Confidence: 0.6988261

 $00{:}55{:}51{.}994 \dashrightarrow 00{:}55{:}54{.}588$ also kind of sides to that because the

NOTE Confidence: 0.6988261

 $00:55:54.588 \rightarrow 00:55:57.048$ unmodified form is targeted for degradation.

NOTE Confidence: 0.6988261

00:55:57.050 --> 00:55:59.866 So I think you know for you guys

NOTE Confidence: 0.6988261

 $00{:}55{:}59{.}866 \dashrightarrow 00{:}56{:}02{.}638$ that you know the pathology and.

NOTE Confidence: 0.6988261

00:56:02.640 --> 00:56:04.383 You know, I think there's a great

NOTE Confidence: 0.6988261

 $00{:}56{:}04{.}383 \dashrightarrow 00{:}56{:}06{.}242$ deal of appreciation on, you know,

NOTE Confidence: 0.6988261

 $00:56:06.242 \rightarrow 00:56:09.008$ let's run next gene sequencing transcriptome

NOTE Confidence: 0.6988261

 $00{:}56{:}09{.}008 \dashrightarrow 00{:}56{:}12{.}057$ and then getting a proteome analysis.

NOTE Confidence: 0.90287343

 $00{:}56{:}14.180 \dashrightarrow 00{:}56{:}15.540$ I think would be great.

NOTE Confidence: 0.90287343

 $00:56:15.540 \rightarrow 00:56:17.871$ You also have the eppi tyranny transcriptome

NOTE Confidence: 0.90287343

 $00:56:17.871 \rightarrow 00:56:20.819$ in some of those disease phenotypes right?

00:56:20.820 --> 00:56:24.250 Like I bet you will be altered.

NOTE Confidence: 0.90287343

 $00{:}56{:}24.250 \dashrightarrow 00{:}56{:}26.162$ There are different modifications

NOTE Confidence: 0.90287343

 $00{:}56{:}26{.}162 \dashrightarrow 00{:}56{:}29{.}572$ like cuisine is one that it's highly

NOTE Confidence: 0.90287343

 $00{:}56{:}29{.}572 \dashrightarrow 00{:}56{:}31{.}887$ evolved on nutritional status and

NOTE Confidence: 0.90287343

00:56:31.887 --> 00:56:34.904 in associated with a whole slew

NOTE Confidence: 0.90287343

 $00{:}56{:}34{.}904 \dashrightarrow 00{:}56{:}37{.}080$ of different disease phenotypes.

NOTE Confidence: 0.90287343

 $00:56:37.080 \longrightarrow 00:56:44.784$ So. How they do so? One way is.

NOTE Confidence: 0.90287343

 $00{:}56{:}44.790 \dashrightarrow 00{:}56{:}48.350$ Depending on the seller response.

NOTE Confidence: 0.90287343

00:56:48.350 --> 00:56:51.050 T RNA is playing a role

NOTE Confidence: 0.90287343

00:56:51.050 - 00:56:52.850 because expression of genes,

NOTE Confidence: 0.90287343

 $00:56:52.850 \dashrightarrow 00:56:54.914$ for example stress response.

NOTE Confidence: 0.90287343

 $00{:}56{:}54{.}914 \dashrightarrow 00{:}56{:}58{.}548$ It is known that genes involved in

NOTE Confidence: 0.90287343

 $00{:}56{:}58{.}548 \dashrightarrow 00{:}57{:}01{.}705$ stress response they have a codon bias,

NOTE Confidence: 0.90287343

 $00{:}57{:}01.710 \dashrightarrow 00{:}57{:}05.455$ so codons that require TNA that is

NOTE Confidence: 0.90287343

 $00{:}57{:}05{.}455 \dashrightarrow 00{:}57{:}08{.}282$ modified are necessary for translation

 $00:57:08.282 \rightarrow 00:57:12.290$ of those of those proteins and evolving

NOTE Confidence: 0.90287343

00:57:12.290 --> 00:57:15.170 in stress response for diabetes,

NOTE Confidence: 0.90287343

 $00{:}57{:}15{.}170 \dashrightarrow 00{:}57{:}18{.}541$ for instance the MS2I6A.

NOTE Confidence: 0.90287343

00:57:18.541 --> 00:57:21.296 What was known is that

NOTE Confidence: 0.90287343

00:57:21.296 --> 00:57:22.949 for insulin translation.

NOTE Confidence: 0.90287343

 $00{:}57{:}22{.}950 \dashrightarrow 00{:}57{:}25{.}734$ You require you have a codon bias towards

NOTE Confidence: 0.90287343

 $00{:}57{:}25{.}734 \dashrightarrow 00{:}57{:}28{.}807$ T RNA that carries that modification.

NOTE Confidence: 0.90287343

 $00:57:28.810 \rightarrow 00:57:31.554$ So if you don't have the modification,

NOTE Confidence: 0.90287343

 $00{:}57{:}31{.}560 \dashrightarrow 00{:}57{:}35{.}130$ then you're compromising translation of

NOTE Confidence: 0.90287343

 $00:57:35.130 \dashrightarrow 00:57:38.210$ of the proteins that depend on that.

NOTE Confidence: 0.90287343

 $00:57:38.210 \longrightarrow 00:57:40.258$ Does that make sense?

NOTE Confidence: 0.90287343

 $00:57:40.258 \longrightarrow 00:57:41.480$ Yeah, good question.

NOTE Confidence: 0.39195618

 $00:57:47.920 \longrightarrow 00:57:50.074$ See any of the benefits

NOTE Confidence: 0.39195618

 $00{:}57{:}50{.}074 \dashrightarrow 00{:}57{:}51{.}958$ that you described utilized

NOTE Confidence: 0.39195618

 $00:57:51.958 \longrightarrow 00:57:54.338$ development for material, yeah.

NOTE Confidence: 0.39195618

 $00:57:54.338 \rightarrow 00:57:56.774$ So there there's a good understanding

- NOTE Confidence: 0.39195618
- $00:57:56.774 \rightarrow 00:57:59.020$ much more on the operatic front.

 $00:57:59.020 \longrightarrow 00:58:00.016$ But for a bacteria,

NOTE Confidence: 0.39195618

 $00:58:00.016 \rightarrow 00:58:02.040$ I think there has been some attempts,

NOTE Confidence: 0.39195618

 $00:58:02.040 \rightarrow 00:58:04.608$ especially for modifications that

NOTE Confidence: 0.39195618

 $00:58:04.608 \longrightarrow 00:58:07.818$ are essential to target the.

NOTE Confidence: 0.39195618

 $00:58:07.820 \longrightarrow 00:58:10.196$ To target those writers,

NOTE Confidence: 0.39195618

00:58:10.196 --> 00:58:11.978 like tyranny writers,

NOTE Confidence: 0.39195618

 $00:58:11.980 \longrightarrow 00:58:13.790$ as a mechanism to hold.

NOTE Confidence: 0.468091815

 $00:58:15.930 \longrightarrow 00:58:20.242$ So viability but that is

NOTE Confidence: 0.468091815

00:58:20.242 --> 00:58:22.666 still kind of in its infancy.

NOTE Confidence: 0.468091815

 $00{:}58{:}22.670 \dashrightarrow 00{:}58{:}24.926$ There's a great deal of interest

NOTE Confidence: 0.468091815

 $00{:}58{:}24{.}926 \dashrightarrow 00{:}58{:}27{.}421$ more recent one up may be targeting

NOTE Confidence: 0.468091815

 $00:58:27.421 \rightarrow 00:58:30.163$ the system itself races because they

NOTE Confidence: 0.468091815

00:58:30.163 - 00:58:32.780 have they are so specific right.

NOTE Confidence: 0.468091815

 $00{:}58{:}32{.}780 \dashrightarrow 00{:}58{:}35{.}147$ So if you can just drop the function of

 $00:58:35.147 \rightarrow 00:58:37.456$ those sustained itself races and that's

NOTE Confidence: 0.468091815

00:58:37.456 --> 00:58:39.951 specific super transfer event then you

NOTE Confidence: 0.468091815

 $00:58:39.951 \rightarrow 00:58:41.727$ selectively inhibit those enzymes.

NOTE Confidence: 0.468091815

00:58:41.730 --> 00:58:43.626 So I don't really do drug

NOTE Confidence: 0.468091815

 $00:58:43.626 \rightarrow 00:58:45.540$ development you know my research.

NOTE Confidence: 0.468091815

00:58:45.540 --> 00:58:48.606 Like as you can tell is more

NOTE Confidence: 0.468091815

 $00{:}58{:}48.610 \dashrightarrow 00{:}58{:}51.020$ kind of fundamental basic science

NOTE Confidence: 0.468091815

 $00:58:51.020 \rightarrow 00:58:52.466$ understanding biochemical pathways.

NOTE Confidence: 0.468091815

 $00{:}58{:}52{.}470 \dashrightarrow 00{:}58{:}55{.}536$ But hopefully you know they're being

NOTE Confidence: 0.468091815

 $00{:}58{:}55{.}536$ --> $00{:}58{:}57{.}580$ interested from pharmaceutical companies

NOTE Confidence: 0.468091815

 $00:58:57.650 \rightarrow 00:58:59.858$ on talking about let's trying to

NOTE Confidence: 0.468091815

 $00:58:59.858 \rightarrow 00:59:01.604$ find an inhibitor especially liking

NOTE Confidence: 0.468091815

 $00{:}59{:}01{.}604 \dashrightarrow 00{:}59{:}03{.}823$ but still is and other gram positive

NOTE Confidence: 0.468091815

00:59:03.823 --> 00:59:05.671 because you have multiple enzymes and

NOTE Confidence: 0.468091815

 $00:59:05.671 \dashrightarrow 00:59:07.770$ then they have very specific phenotypes.

NOTE Confidence: 0.468091815

 $00:59:07.770 \longrightarrow 00:59:10.682$ Can we find any inhibitor that binds to

- NOTE Confidence: 0.468091815
- $00{:}59{:}10.682 \dashrightarrow 00{:}59{:}13.730$ like only so fast that is found in Gram
- NOTE Confidence: 0.468091815
- $00{:}59{:}13.730 \dashrightarrow 00{:}59{:}16.229$ positive as a specialized drug development.
- NOTE Confidence: 0.468091815
- $00:59:16.229 \longrightarrow 00:59:18.794$ So antibiotic that targets only
- NOTE Confidence: 0.468091815
- $00{:}59{:}18.794 \dashrightarrow 00{:}59{:}21.130$ grandparent grand positive pathogens.
- NOTE Confidence: 0.468091815
- 00:59:21.130 --> 00:59:21.700 Yeah.
- NOTE Confidence: 0.82425005
- 00:59:26.550 --> 00:59:29.000 Good, OK.