WEBVTT

NOTE duration: ”00:03:56.032”

NOTE Confidence: 0.9961058

00:00:04.880 --> 00:00:05.380 Mycobacteria

NOTE Confidence: 0.96761817

00:00:05.759 --> 00:00:07.299 are a group of bacteria

NOTE Confidence: 0.96761817

00:00:07.440 --> 00:00:08.800 and there's lots of different

NOTE Confidence: 0.96761817

00:00:08.800 --> 00:00:09.300 types.

NOTE Confidence: 0.97688484

00:00:09.920 --> 00:00:11.119 Many of them are found

NOTE Confidence: 0.97688484

00:00:11.119 --> 00:00:12.480 in soil and water and

NOTE Confidence: 0.97688484

00:00:12.480 --> 00:00:13.540 are essentially harmless

NOTE Confidence: 0.9717162

00:00:13.855 --> 00:00:15.535 to most people. But there

NOTE Confidence: 0.9717162

00:00:15.535 --> 00:00:16.914 are a few mycobacteria

NOTE Confidence: 0.9611937

00:00:17.375 --> 00:00:18.994 that actually cause very devastating

NOTE Confidence: 0.9611937

00:00:19.055 --> 00:00:20.494 human diseases and one of

NOTE Confidence: 0.9611937

00:00:20.494 --> 00:00:21.715 the most famous is mycobacterium

NOTE Confidence: 0.9611937

00:00:21.935 --> 00:00:22.435 tuberculosis

NOTE Confidence: 0.8916495

00:00:22.735 --> 00:00:23.875 which causes tuberculosis.

NOTE Confidence: 0.9242846

00:00:24.575 --> 00:00:26.595 There's another mycobacteria called mycobacterium

NOTE Confidence: 0.9242846

00:00:26.814 --> 00:00:28.390 leprae that cause the disease

NOTE Confidence: 0.9242846

00:00:28.390 --> 00:00:28.890 leprosy.

NOTE Confidence: 0.948384

00:00:35.030 --> 00:00:36.570 There are several unique features.

NOTE Confidence: 0.948384

00:00:36.870 --> 00:00:38.309 First is that different from

NOTE Confidence: 0.948384

00:00:38.309 --> 00:00:39.670 other bacteria it has a

NOTE Confidence: 0.948384

00:00:39.670 --> 00:00:41.745 very unusual cell wall or

NOTE Confidence: 0.948384

00:00:41.745 --> 00:00:43.125 cell envelope architecture.

NOTE Confidence: 0.9569767

00:00:44.065 --> 00:00:45.505 And the cell envelope is

NOTE Confidence: 0.9569767

00:00:45.505 --> 00:00:47.265 basically the thing that coats

NOTE Confidence: 0.9569767

00:00:47.265 --> 00:00:49.104 the bacterium and protects it

NOTE Confidence: 0.9569767

00:00:49.104 --> 00:00:49.845 and interfaces

NOTE Confidence: 0.9993569

00:00:50.225 --> 00:00:51.045 with the environment.

NOTE Confidence: 0.99479073

00:00:51.585 --> 00:00:52.085 Mycobacteria

NOTE Confidence: 0.9988148

00:00:52.465 --> 00:00:53.445 have a very unusual

NOTE Confidence: 0.9734975

00:00:54.145 --> 00:00:55.825 structure to its cell envelope.

NOTE Confidence: 0.9734975

00:00:55.825 --> 00:00:57.100 It's very thick, it's very

NOTE Confidence: 0.9734975

00:00:57.100 --> 00:00:58.700 waxy, and we think that

NOTE Confidence: 0.9734975

00:00:58.700 --> 00:00:59.900 that prevents a lot of

NOTE Confidence: 0.9734975

00:00:59.900 --> 00:01:01.420 antibiotics from actually getting into

NOTE Confidence: 0.9734975

00:01:01.420 --> 00:01:02.160 the bacterium

NOTE Confidence: 0.9897867

00:01:02.540 --> 00:01:03.820 to reach their target and

NOTE Confidence: 0.9897867

00:01:03.820 --> 00:01:05.340 to kill the bacterium. And

NOTE Confidence: 0.9897867

00:01:05.340 --> 00:01:06.459 then the second feature that

NOTE Confidence: 0.9897867

00:01:06.459 --> 00:01:07.500 we think is really unusual

NOTE Confidence: 0.9897867

00:01:07.500 --> 00:01:08.080 to mycobacteria

NOTE Confidence: 0.98668987

00:01:08.395 --> 00:01:09.295 is that even

NOTE Confidence: 0.96375597

00:01:09.834 --> 00:01:12.015 in a genetically identical population,

NOTE Confidence: 0.99599916

00:01:12.715 --> 00:01:14.475 mycobacteria seem very good at

NOTE Confidence: 0.99599916

00:01:14.475 --> 00:01:15.935 generating a lot of diversity

NOTE Confidence: 0.99291664

00:01:16.555 --> 00:01:17.855 in different physiological

NOTE Confidence: 0.9991304

00:01:18.475 --> 00:01:18.975 properties.

NOTE Confidence: 0.9550512

00:01:19.834 --> 00:01:21.275 We think that differences in

NOTE Confidence: 0.9550512

00:01:21.275 --> 00:01:22.175 in these mycobacterial

NOTE Confidence: 0.995783

00:01:22.680 --> 00:01:23.959 populations at the single cell

NOTE Confidence: 0.995783

00:01:23.959 --> 00:01:25.900 level can be really important

NOTE Confidence: 0.995783

00:01:26.040 --> 00:01:27.100 for the bacteria

NOTE Confidence: 0.96320415

00:01:27.959 --> 00:01:30.280 to tolerate antibiotics, meaning that

NOTE Confidence: 0.96320415

00:01:30.280 --> 00:01:31.260 there are some bacteria

NOTE Confidence: 0.99791574

00:01:31.800 --> 00:01:34.220 that can survive antibiotic pressure

NOTE Confidence: 0.9835254

00:01:34.600 --> 00:01:35.980 simply because they phenotypically

NOTE Confidence: 0.9990178

00:01:36.360 --> 00:01:37.560 look a little different than

NOTE Confidence: 0.9990178

00:01:37.560 --> 00:01:37.995 others.

NOTE Confidence: 0.9686452

00:01:39.275 --> 00:01:41.135 How are individual mycobacteria

NOTE Confidence: 0.9883052

00:01:41.435 --> 00:01:42.635 different? How do they differ

NOTE Confidence: 0.9883052

00:01:42.635 --> 00:01:44.175 in the responses to antibiotics?

NOTE Confidence: 0.9883052

00:01:44.395 --> 00:01:45.834 What are the underlying causes

NOTE Confidence: 0.9883052

00:01:45.834 --> 00:01:46.735 of those differences?

NOTE Confidence: 0.98401016

00:01:47.115 --> 00:01:47.915 We think a lot of

NOTE Confidence: 0.98401016

00:01:47.915 --> 00:01:49.455 it traces down to metabolism

NOTE Confidence: 0.98401016

00:01:49.675 --> 00:01:50.490 and so my lab is

NOTE Confidence: 0.98401016

00:01:50.490 --> 00:01:52.090 really trying to understand the

NOTE Confidence: 0.98401016

00:01:52.090 --> 00:01:52.590 metabolism

NOTE Confidence: 0.99396867

00:01:53.050 --> 00:01:54.430 of individual mycobacteria.

NOTE Confidence: 0.99329513

00:02:00.330 --> 00:02:01.930 We use microscopes to answer

NOTE Confidence: 0.99329513

00:02:01.930 --> 00:02:02.670 those questions.

NOTE Confidence: 0.9695163

00:02:03.610 --> 00:02:05.210 That can range from simple

NOTE Confidence: 0.9695163

00:02:05.210 --> 00:02:07.185 time lapse videos where we

NOTE Confidence: 0.9695163

00:02:07.185 --> 00:02:09.105 look at individual cells over

NOTE Confidence: 0.9695163

00:02:09.105 --> 00:02:10.625 time. And because some of

NOTE Confidence: 0.9695163

00:02:10.625 --> 00:02:11.585 them can grow and divide

NOTE Confidence: 0.9695163

00:02:11.585 --> 00:02:12.625 really slowly, we have to

NOTE Confidence: 0.9695163

00:02:12.625 --> 00:02:13.665 run our microscopes for up

NOTE Confidence: 0.9695163

00:02:13.665 --> 00:02:14.785 to five days in order

NOTE Confidence: 0.9695163

00:02:14.785 --> 00:02:15.264 to,

NOTE Confidence: 0.93092847

00:02:15.665 --> 00:02:17.425 capture the cell growth and

NOTE Confidence: 0.93092847

00:02:17.425 --> 00:02:18.625 and division of these of

NOTE Confidence: 0.93092847

00:02:18.625 --> 00:02:20.090 these organisms. But we also

NOTE Confidence: 0.93092847

00:02:20.090 --> 00:02:22.330 use, super resolution microscopy to

NOTE Confidence: 0.93092847

00:02:22.330 --> 00:02:24.270 understand the spatial organization

NOTE Confidence: 0.9980701

00:02:24.810 --> 00:02:26.669 of proteins within the cell.

NOTE Confidence: 0.9559218

00:02:27.210 --> 00:02:28.570 We also started using these

NOTE Confidence: 0.9559218

00:02:28.570 --> 00:02:30.669 fluorescent reporters or sensors

NOTE Confidence: 0.99664295

00:02:31.210 --> 00:02:33.450 for different metabolic properties of

NOTE Confidence: 0.99664295

00:02:33.450 --> 00:02:34.065 the cell.

NOTE Confidence: 0.9857854

00:02:34.544 --> 00:02:35.985 For example, we have used

NOTE Confidence: 0.9857854

00:02:35.985 --> 00:02:38.405 a fluorescent reporter for, ATP,

NOTE Confidence: 0.9857854

00:02:38.465 --> 00:02:39.905 which is the energy currency

NOTE Confidence: 0.9857854

00:02:39.905 --> 00:02:40.705 of the cell. And so

NOTE Confidence: 0.9857854

00:02:40.705 --> 00:02:42.385 now we can measure ATP

NOTE Confidence: 0.9857854

00:02:42.385 --> 00:02:42.885 levels

NOTE Confidence: 0.9903931

00:02:43.264 --> 00:02:45.605 in individual cells, and understand

NOTE Confidence: 0.9903931

00:02:45.825 --> 00:02:47.825 how differences in in,

NOTE Confidence: 0.9712527

00:02:48.145 --> 00:02:49.764 say, ATP or other metabolites

NOTE Confidence: 0.9712527

00:02:50.040 --> 00:02:51.639 are generated in a clonal

NOTE Confidence: 0.9712527

00:02:51.639 --> 00:02:53.079 population and what are the

NOTE Confidence: 0.9712527

00:02:53.079 --> 00:02:55.319 consequences for having different levels

NOTE Confidence: 0.9712527

00:02:55.319 --> 00:02:56.459 of of these metabolites.

NOTE Confidence: 0.9927048

00:03:02.995 --> 00:03:04.915 Our goals are treating some

NOTE Confidence: 0.9927048

00:03:04.915 --> 00:03:05.655 of these mycobacterial

NOTE Confidence: 0.9956703

00:03:05.955 --> 00:03:06.455 infections.

NOTE Confidence: 0.9993697

00:03:06.915 --> 00:03:07.415 Tuberculosis

NOTE Confidence: 0.9633178

00:03:08.035 --> 00:03:09.235 kills more people each year

NOTE Confidence: 0.9633178

00:03:09.235 --> 00:03:10.935 than any other single infectious

NOTE Confidence: 0.9633178

00:03:10.995 --> 00:03:12.435 disease, and in history has

NOTE Confidence: 0.9633178

00:03:12.435 --> 00:03:13.715 actually killed more people than

NOTE Confidence: 0.9633178

00:03:13.715 --> 00:03:15.669 any single infectious disease. So

NOTE Confidence: 0.9633178

00:03:15.669 --> 00:03:17.669 it's an incredible global health

NOTE Confidence: 0.9633178

00:03:17.669 --> 00:03:18.169 problem.

NOTE Confidence: 0.9632236

00:03:19.270 --> 00:03:20.810 If someone gets TB,

NOTE Confidence: 0.97946966

00:03:21.190 --> 00:03:21.910 they have to go on

NOTE Confidence: 0.97946966

00:03:21.910 --> 00:03:23.450 a course of antibiotic therapy

NOTE Confidence: 0.97946966

00:03:23.590 --> 00:03:25.030 that can last anywhere from

NOTE Confidence: 0.97946966

00:03:25.030 --> 00:03:26.310 four to six months with

NOTE Confidence: 0.97946966

00:03:26.310 --> 00:03:26.889 a combination

NOTE Confidence: 0.9273908

00:03:27.190 --> 00:03:28.605 of four antibiotics,

NOTE Confidence: 0.99222463

00:03:29.065 --> 00:03:30.105 which as you can imagine

NOTE Confidence: 0.99222463

00:03:30.105 --> 00:03:31.305 is a very long time

NOTE Confidence: 0.99222463

00:03:31.305 --> 00:03:32.845 to be on antibiotic therapy.

NOTE Confidence: 0.9879161

00:03:34.025 --> 00:03:35.225 We think that if there

NOTE Confidence: 0.9879161

00:03:35.225 --> 00:03:36.205 are all these differences

NOTE Confidence: 0.96185493

00:03:36.505 --> 00:03:37.485 in metabolism

NOTE Confidence: 0.99825335

00:03:37.865 --> 00:03:38.605 and physiology

NOTE Confidence: 0.9801264

00:03:39.545 --> 00:03:41.245 of that bacterial population,

NOTE Confidence: 0.9975317

00:03:42.170 --> 00:03:43.129 then we think that if

NOTE Confidence: 0.9975317

00:03:43.129 --> 00:03:44.430 we can transition

NOTE Confidence: 0.9593841

00:03:44.890 --> 00:03:47.050 cells or force cells into

NOTE Confidence: 0.9593841

00:03:47.050 --> 00:03:49.129 a more antibiotic favorable state

NOTE Confidence: 0.9593841

00:03:49.129 --> 00:03:50.010 that we might be able

NOTE Confidence: 0.9593841

00:03:50.010 --> 00:03:51.450 to treat an infection more

NOTE Confidence: 0.9593841

00:03:51.450 --> 00:03:51.950 rapidly.