WEBVTT

NOTE duration: "00:03:31.968"

NOTE Confidence: 0.98466295

00:00:05.359 --> 00:00:06.899 The skin is the largest

NOTE Confidence: 0.98466295

00:00:07.040 --> 00:00:08.639 organ in the body. And

NOTE Confidence: 0.98466295

00:00:08.639 --> 00:00:09.679 not only is it a

NOTE Confidence: 0.98466295

00:00:09.679 --> 00:00:10.960 barrier, but it has a

NOTE Confidence: 0.98466295

00:00:10.960 --> 00:00:12.875 very active immune system. When

NOTE Confidence: 0.98466295

00:00:12.875 --> 00:00:14.014 we think of inflammatory

NOTE Confidence: 0.9832467

00:00:14.315 --> 00:00:16.154 skin disorders, psoriasis, when we

NOTE Confidence: 0.9832467

00:00:16.154 --> 00:00:17.994 think of atopic dermatitis, they

NOTE Confidence: 0.9832467

00:00:17.994 --> 00:00:19.195 all have a component of

NOTE Confidence: 0.9832467

00:00:19.195 --> 00:00:20.414 skin barrier disruption.

NOTE Confidence: 0.99636734

00:00:20.794 --> 00:00:21.755 And so many of the

NOTE Confidence: 0.99636734

00:00:21.755 --> 00:00:23.595 diseases in dermatology become a

NOTE Confidence: 0.99636734

00:00:23.595 --> 00:00:25.994 vicious cycle between skin barrier

NOTE Confidence: 0.99636734

00:00:25.994 --> 00:00:27.454 disruption and inflammation.

NOTE Confidence: 0.9948054

00:00:28.300 --> 00:00:30.380 Patients also experience things like

NOTE Confidence: 0.9948054

00:00:30.380 --> 00:00:30.880 itch,

NOTE Confidence: 0.9883549

00:00:31.260 --> 00:00:33.340 burning, stinging, and it affects

NOTE Confidence: 0.9883549

00:00:33.340 --> 00:00:34.940 their quality of life. And

NOTE Confidence: 0.9883549

00:00:34.940 --> 00:00:36.320 my job as the scientist

NOTE Confidence: 0.9883549

00:00:36.540 --> 00:00:38.300 is understanding how to break

NOTE Confidence: 0.9883549

00:00:38.300 --> 00:00:39.280 this loop.

NOTE Confidence: 0.9759062

00:00:45.575 --> 00:00:46.935 In the big picture, my

NOTE Confidence: 0.9759062

00:00:46.935 --> 00:00:48.375 laboratory is doing what is

NOTE Confidence: 0.9759062

00:00:48.375 --> 00:00:50.375 called structural biology. We are

NOTE Confidence: 0.9759062

00:00:50.375 --> 00:00:52.075 trying to understand the structure

NOTE Confidence: 0.9759062

00:00:52.215 --> 00:00:53.595 of how proteins,

NOTE Confidence: 0.9873749

00:00:54.055 --> 00:00:55.910 nucleic acids, and other macromolecules

NOTE Confidence: 0.97278315

00:00:56.449 --> 00:00:57.969 work in the skin and

NOTE Confidence: 0.97278315

00:00:57.969 --> 00:00:59.969 how drugs that target different

NOTE Confidence: 0.97278315

00:00:59.969 --> 00:01:01.969 skin diseases work. And then

NOTE Confidence: 0.97278315

00:01:01.969 --> 00:01:03.730 in certain genetic diseases where

NOTE Confidence: 0.97278315

00:01:03.730 --> 00:01:04.869 those proteins

NOTE Confidence: 0.99069744

00:01:05.170 --> 00:01:06.770 are in error, we want

NOTE Confidence: 0.99069744

00:01:06.770 --> 00:01:08.130 to understand what has gone

NOTE Confidence: 0.99069744

00:01:08.130 --> 00:01:09.409 wrong and how can we

NOTE Confidence: 0.99069744

00:01:09.409 --> 00:01:09.735 fix

NOTE Confidence: 0.99456376

00:01:10.535 --> 00:01:11.575 it. There's no one else

NOTE Confidence: 0.99456376

00:01:11.575 --> 00:01:12.315 in dermatology

NOTE Confidence: 0.9929727

00:01:12.855 --> 00:01:14.315 that is running a primary

NOTE Confidence: 0.9929727

00:01:14.375 --> 00:01:16.935 NIH funded research lab that's

NOTE Confidence: 0.9929727

00:01:16.935 --> 00:01:18.855 dedicated to structural biology and

NOTE Confidence: 0.9929727

00:01:18.855 --> 00:01:20.075 answering those difficult

NOTE Confidence: 0.9995214

00:01:20.375 --> 00:01:20.875 biochemistry

NOTE Confidence: 0.9415083

00:01:21.175 --> 00:01:23.255 questions through the approaches of

NOTE Confidence: 0.9415083

00:01:23.255 --> 00:01:24.075 extra crystallography,

NOTE Confidence: 0.96317565

00:01:24.880 --> 00:01:26.880 cryo electron microscopy, and if

NOTE Confidence: 0.96317565

00:01:26.880 --> 00:01:29.459 needed, nuclear magnetic resonance imaging.

NOTE Confidence: 0.90512323

00:01:33.440 --> 00:01:34.660 So extra crystallography

NOTE Confidence: 0.992693

00:01:35.040 --> 00:01:36.560 is a particular technique that

NOTE Confidence: 0.992693

00:01:36.560 --> 00:01:37.600 allows you to understand the

NOTE Confidence: 0.992693

00:01:37.600 --> 00:01:39.045 atomic level structure

NOTE Confidence: 0.98488617

00:01:39.604 --> 00:01:41.765 of proteins, nucleic acids, and

NOTE Confidence: 0.98488617

00:01:41.765 --> 00:01:42.505 their complexes.

NOTE Confidence: 0.9964226

00:01:43.525 --> 00:01:44.325 What you have to do

NOTE Confidence: 0.9964226

00:01:44.325 --> 00:01:45.685 in crystallography is take a

NOTE Confidence: 0.9964226

00:01:45.685 --> 00:01:47.705 very pure protein, for example,

NOTE Confidence: 0.9964226

00:01:47.765 --> 00:01:48.645 and put it in the

NOTE Confidence: 0.9964226

00:01:48.645 --> 00:01:49.545 right solution

NOTE Confidence: 0.99620914

00:01:49.845 --> 00:01:51.145 that allows it to precipitate.

NOTE Confidence: 0.98361063

00:01:51.924 --> 00:01:52.965 And when it does it

NOTE Confidence: 0.98361063

00:01:52.965 --> 00:01:54.325 just right, it forms a

NOTE Confidence: 0.98361063

00:01:54.325 --> 00:01:56.460 crystal. And that crystal is

NOTE Confidence: 0.98361063

00:01:56.460 --> 00:01:57.200 a perfectly

NOTE Confidence: 0.9808655

00:01:57.500 --> 00:01:59.820 aligned lattice of lots and

NOTE Confidence: 0.9808655

00:01:59.820 --> 00:02:01.179 lots of molecules of that

NOTE Confidence: 0.9808655

00:02:01.179 --> 00:02:02.539 protein of interest. And then

NOTE Confidence: 0.9808655

00:02:02.539 --> 00:02:04.000 when you hit that crystal

NOTE Confidence: 0.9808655

00:02:04.219 --> 00:02:06.140 with x rays, that crystal

NOTE Confidence: 0.9808655

00:02:06.140 --> 00:02:07.119 then diffracts

NOTE Confidence: 0.9925673

00:02:07.435 --> 00:02:08.715 the light. And then what

NOTE Confidence: 0.9925673

00:02:08.715 --> 00:02:09.514 we can do is use

NOTE Confidence: 0.9925673

00:02:09.514 --> 00:02:10.014 mathematical

NOTE Confidence: 0.98380727

00:02:10.315 --> 00:02:11.855 approaches to take that diffraction

NOTE Confidence: 0.98380727

00:02:11.915 --> 00:02:13.595 pattern and turn it into

NOTE Confidence: 0.98380727

00:02:13.595 --> 00:02:14.655 actually a three-dimensional

NOTE Confidence: 0.99983895

00:02:15.115 --> 00:02:15.615 model

NOTE Confidence: 0.9788263

00:02:15.915 --> 00:02:17.435 of that protein, and that

NOTE Confidence: 0.9788263

00:02:17.435 --> 00:02:18.715 allows us to determine the

NOTE Confidence: 0.9788263

00:02:18.715 --> 00:02:19.995 structure at that atom and

NOTE Confidence: 0.9788263

00:02:19.995 --> 00:02:21.355 bond level. And then we

NOTE Confidence: 0.9788263

00:02:21.355 --> 00:02:22.710 can take that information and

NOTE Confidence: 0.9788263

00:02:22.710 --> 00:02:24.630 ask those critical questions. What

NOTE Confidence: 0.9788263

00:02:24.630 --> 00:02:25.830 does this tell us about

NOTE Confidence: 0.9788263

00:02:25.830 --> 00:02:27.210 helping the human patient?

NOTE Confidence: 0.96867526

00:02:33.030 --> 00:02:34.389 One of the wonderful things

NOTE Confidence: 0.96867526

00:02:34.389 --> 00:02:35.990 about being a physician scientist

NOTE Confidence: 0.96867526

00:02:35.990 --> 00:02:36.790 is I get to see

NOTE Confidence: 0.96867526

00:02:36.790 --> 00:02:37.965 what it's like in the

NOTE Confidence: 0.96867526

00:02:38.364 --> 00:02:39.584 lab to make a discovery,

NOTE Confidence: 0.96867526

00:02:39.724 --> 00:02:40.605 but I also get to

NOTE Confidence: 0.96867526

00:02:40.605 --> 00:02:41.805 talk to patients face to

NOTE Confidence: 0.96867526

00:02:41.805 --> 00:02:43.165 face. And I really get

NOTE Confidence: 0.96867526

00:02:43.165 --> 00:02:45.025 an understanding of what matters

NOTE Confidence: 0.96867526

00:02:45.165 --> 00:02:45.905 to them.

NOTE Confidence: 0.9940075

00:02:46.205 --> 00:02:47.405 And the advantage of this

NOTE Confidence: 0.9940075

00:02:47.405 --> 00:02:48.444 is it allows me to

NOTE Confidence: 0.9940075

00:02:48.444 --> 00:02:49.805 then come back from a

NOTE Confidence: 0.9940075

00:02:49.805 --> 00:02:51.905 translational perspective and understand

NOTE Confidence: 0.9992671

00:02:52.205 --> 00:02:53.665 what is going to help

NOTE Confidence: 0.99552894

00:02:54.180 --> 00:02:56.500 deliver better patient care. This

NOTE Confidence: 0.99552894

00:02:56.500 --> 00:02:57.860 is also why I really

NOTE Confidence: 0.99552894

00:02:57.860 --> 00:02:58.820 am excited to be a

NOTE Confidence: 0.99552894

00:02:58.820 --> 00:03:00.419 part of clinical trials here

NOTE Confidence: 0.99552894

00:03:00.419 --> 00:03:01.000 in dermatology

NOTE Confidence: 0.9989852

00:03:01.300 --> 00:03:01.960 at Yale.

NOTE Confidence: 0.99570644

00:03:03.220 --> 00:03:05.139 I love helping patients. I

NOTE Confidence: 0.99570644

00:03:05.139 --> 00:03:06.740 love it when patients feel

NOTE Confidence: 0.99570644

00:03:06.740 --> 00:03:08.100 better and are happier with

NOTE Confidence: 0.99570644

00:03:08.100 --> 00:03:08.600 themselves.

NOTE Confidence: 0.99634796

00:03:08.980 --> 00:03:10.284 In the end, all of

NOTE Confidence: 0.99634796

00:03:10.284 --> 00:03:11.405 what we do, whether it's

NOTE Confidence: 0.99634796

00:03:11.405 --> 00:03:12.465 the research mission,

NOTE Confidence: 0.9935456

00:03:12.764 --> 00:03:14.125 the clinical mission, or even

NOTE Confidence: 0.9935456

00:03:14.125 --> 00:03:15.724 a clinical trial mission, it's

NOTE Confidence: 0.9935456

00:03:15.724 --> 00:03:18.144 all about advancing patient care,

NOTE Confidence: 0.9935456

00:03:18.204 --> 00:03:19.965 developing new therapies for rare

NOTE Confidence: 0.9935456

00:03:19.965 --> 00:03:21.644 genetic skin diseases for which

NOTE Confidence: 0.9935456

00:03:21.644 --> 00:03:23.264 patients have nothing yet.