WEBVTT

00:00:05.630 --> 00:00:07.716 Inborn errors of immunity is an umbrella term we think about

00:00:07.716 --> 00:00:10.427 for these primarily pediatric immune disorders

00:00:10.719 --> 00:00:14.180 and the way I like to think about it is these are genetic diseases.

00:00:14.180 --> 00:00:16.099 If you think about all humans on Earth

00:00:16.099 --> 00:00:18.059 as being sort of part of a bell curve, right,

00:00:18.059 --> 00:00:19.769 in terms of your immune responsiveness.

00:00:19.769 --> 00:00:21.229 We like to study the extremes.

00:00:21.563 --> 00:00:24.232 So the kids who have really low immune function

00:00:24.232 --> 00:00:25.900 and therefore get a lot of infections,

00:00:26.735 --> 00:00:27.986 and also the kids on the other side of the bell curve

00:00:27.986 --> 00:00:29.779 who have a really high immune response

00:00:29.779 --> 00:00:30.864 and rather than infection,

00:00:30.864 --> 00:00:34.159 they suffer from immune-mediated damage to their tissues.

00:00:39.789 --> 00:00:43.626 So my lab is really excited to learn fundamental immunology

00:00:43.626 --> 00:00:46.212 and really how the immune system works as a system,

00:00:46.212 --> 00:00:48.006 starting first with patients

00:00:48.006 --> 00:00:51.509 and these are primarily pediatric patients who have severe immune diseases.

00:00:51.968 --> 00:00:55.597 But we test the hypothesis these kids could be sick from a single gene mutation

00:00:56.014 --> 00:00:59.893 and then we used models to dissect mechanisms and come up with precision therapies.

00:01:04.105 --> 00:01:05.398 We do genomics.

00:01:05.398 --> 00:01:07.484 So this is where we sequenced the whole genome

00:01:07.484 --> 00:01:09.360 to find that sort of needle in the haystack.

00:01:09.360 --> 00:01:12.072 So if we're right that the hypothesis is true

00:01:12.072 --> 00:01:14.240 that this kid is sick from a single gene mutation,

00:01:14.240 --> 00:01:16.493 we can identify that using genomics.

00:01:17.327 --> 00:01:18.995 And then we also use models.

00:01:18.995 --> 00:01:22.082 So we'll use Crispr to engineer versions of the human mutation

00:01:22.415 --> 00:01:25.627 and then can do all kinds of immunology assays.

00:01:25.835 --> 00:01:28.296 So it allows us to do in vitro work.

00:01:28.296 --> 00:01:31.174 In addition, we do experiments to understand why

00:01:31.174 --> 00:01:34.969 this gene mutation could make their immune cells function abnormally

00:01:35.178 --> 00:01:38.264 and then we also test therapies and things in models

00:01:38.264 --> 00:01:41.851 that our goal then is to translate back into the patients

00:01:42.143 --> 00:01:44.646 and, importantly, it's not just the patients with the rare disease.

00:01:44.646 --> 00:01:48.733 Also, we think that by studying these extremes on the sort of bell curve,

00:01:48.942 --> 00:01:52.821 we're learning fundamental immunobiology that applies to more common diseases

00:01:52.821 --> 00:01:54.656 as well, but maybe in less severe form.

00:02:00.161 --> 00:02:01.204 Precision therapy,

00:02:01.412 --> 00:02:03.206 understanding the gene mutation,

00:02:03.206 --> 00:02:05.834 makes you realize what kind of treatment is best for them.

00:02:05.834 --> 00:02:06.835 So this is where it leads.

00:02:06.835 --> 00:02:09.129 It leads to precision therapy for rare disease.

00:02:09.129 --> 00:02:12.507 But in addition, because we're learning fundamental immunology

00:02:12.507 --> 00:02:15.552 directly from patients, it builds foundational knowledge

00:02:15.552 --> 00:02:18.847 that allows us to spin off new knowledge in ways one can't predict.

00:02:19.055 --> 00:02:22.725 So it can lead to, we think, more well-defined foundations

00:02:22.725 --> 00:02:26.020 about how the human immune system works and how we might manipulate it.

00:02:27.188 --> 00:02:30.441 It's an amazing time to be in medicine and in science,

00:02:30.441 --> 00:02:35.071 where we've got so many different potential therapies on the shelves, right?

00:02:35.071 --> 00:02:39.492 And there are ways we can modulate the immune system in ways that have really, really advanced

00:02:39.492 --> 00:02:42.412 and it's partly matchmaking, trying to understand

00:02:42.412 --> 00:02:45.373 why is this person sick so we can choose the right therapy

00:02:45.373 --> 00:02:48.918 and also innovating around new therapies because as our knowledge expands,

00:02:48.918 --> 00:02:51.754 we can think about how we could rewire these these circuits.