

WEBVTT

00:00:05.255 --> 00:00:08.633 The skin itself is a barrier to the external world.

00:00:08.633 --> 00:00:13.722 You need to be able to respond to things like physical trauma, to pathogens,

00:00:13.722 --> 00:00:17.350 and so it has a remarkable ability to both generate

00:00:17.350 --> 00:00:20.562 and resolve these kind of inflammatory contexts.

00:00:20.979 --> 00:00:26.651 But in the setting of autoimmunity, you're no longer able to turn off that switch.

00:00:26.651 --> 00:00:29.779 At a fundamental level, the body is confused

00:00:29.779 --> 00:00:33.324 and recognizing something as a virus.

00:00:39.289 --> 00:00:42.292 I focus on cutaneous lupus.

00:00:42.292 --> 00:00:46.379 Lupus itself mimics, in some ways, a viral infection.

00:00:46.755 --> 00:00:51.259 The signals that we see in these patients are elevated interferons

00:00:51.259 --> 00:00:55.722 and that's a molecule that is important for fighting off viruses,

00:00:56.723 --> 00:01:00.602 and that's why lupus patients, they may say they have chronic fatigue.

00:01:00.643 --> 00:01:01.811 They feel terrible.

00:01:01.811 --> 00:01:06.316 Well they quite literally are feeling the effects of a viral infection

00:01:06.316 --> 00:01:09.736 because at the molecular level there are considerable similarities.

00:01:10.779 --> 00:01:13.448 One of the major things that we study

00:01:13.448 --> 00:01:15.158 is something called retroelements.

00:01:15.909 --> 00:01:20.121 So these have integrated into our genome over many millions of years

00:01:20.830 --> 00:01:23.833 and they comprise actually about 50% of our genome.

00:01:24.334 --> 00:01:27.629 Normally these elements are epigenetically silent.

00:01:27.629 --> 00:01:29.839 So you don't really see them in normal tissues.

00:01:29.839 --> 00:01:33.676 But in the setting of autoimmunity, they do become transcriptional active.

00:01:34.344 --> 00:01:38.431 We believe the body is recognizing some of these retroelements

00:01:38.431 --> 00:01:40.809 in a capacity that it thinks it's a virus.

00:01:47.315 --> 00:01:49.526 We do use cutting edge technologies like

00:01:49.526 --> 00:01:54.072 single cell RNA sequencing, spatial single cell RNA sequencing,

00:01:54.072 --> 00:01:59.577 and that's really able to kind of map the disease architecture at the cellular level.

00:01:59.577 --> 00:02:03.039 So you're able to get very high resolution information from that.

00:02:03.331 --> 00:02:05.917 Additionally, we take samples from patients

00:02:05.917 --> 00:02:08.711 and we move that into an in vitro setting

00:02:08.711 --> 00:02:12.340 and we're able to deliver specific controlled interventions

00:02:12.340 --> 00:02:15.468 to try to discern like cause and effect molecular mechanisms,

00:02:15.760 --> 00:02:19.347 and additionally we do use genetically engineered models

00:02:19.347 --> 00:02:22.350 that recapitulate certain aspects of human disease

00:02:22.433 --> 00:02:24.978 and, again, in that more controlled environment

00:02:24.978 --> 00:02:28.940 we're able to test specific interventions and see their effect.

00:02:34.529 --> 00:02:37.574 Ultimately, one of the major goals is to

00:02:37.574 --> 00:02:40.910 better understand the source of both the innate

00:02:40.910 --> 00:02:45.790 and adaptive immune signals that manifest as autoimmunity in lupus patients.

00:02:46.374 --> 00:02:50.295 If we're able to better target things upstream and prevent

00:02:50.295 --> 00:02:53.631 that process from happening, perhaps we're better able to get

00:02:53.631 --> 00:02:57.135 precise, targeted therapies that have less side effects for patients.