Meet Shlomo Melmed the 2022 Transatlantic Alliance Awardee

Shlomo Melmed is Executive Vice President of Academic Affairs, Dean of the Medical Faculty and Distinguished Professor of Medicine at Cedars-Sinai in Los Angeles, USA. He is an international authority on pituitary medicine, and the inaugural winner of the Transatlantic Alliance Award. Read on to learn more about his career and research ahead of his ECE 2022 lecture on 'Growth hormone: an adult misnomer'.

Tell us about your current position and research

I've devoted my entire career to pituitary medicine. I lead a pituitary clinic with extremely talented colleagues, who are totally devoted to treating patients with pituitary disorders. We have an integrated pituitary centre including colleagues from neurosurgery, pathology, neuroimaging and radiotherapy. We also perform investigator- and sponsor-initiated clinical trials. I'm very focused on treating patients with pituitary disorders and also have an NIH funded laboratory, where we study mechanisms underlying pituitary hormone production and signalling. We investigate mechanisms sub serving the formation of pituitary tumours using genetic, cellular, animal and human tissue models. Several of the molecules that we have uncovered in the lab have now been translated into active clinical trials.

What more specifically are you presenting at ECE 2022?

I'm going to talk about some of our more recent work on uncovering novel actions for growth hormone. Although we know that growth hormone is required for longitudinal bone growth, we still continue to produce it as adults…and the question is why? Both childhood onset adult growth hormone deficiency and adult onset acquired growth hormone deficiency seem to imply that we still need growth hormone as adults. Adults deficient in growth hormone have a very unique phenotype. They have central obesity, may have high blood pressure and also lethargy. Growth hormone in adulthood is needed to maintain body homeostasis, the correct ratio between lean body mass and fat mass. As we age, growth hormone levels drop dramatically, which raises the question of whether we should continue giving growth hormone to elderly people. Could it reverse the frailty of aging? This has yet

to be proven in clinical trials. However, if you take growth hormone as an adult, and you're not pituitary- deficient, you may lose a few kilogrammes of adipose tissue, but we're not sure if that would be sustained. There's no evidence that lifespan would be extended in any way, and subtle evidence that low growth hormone may in fact benefit health span.

We are studying the action of adult growth hormone on epithelial cells and have found that it is involved in regulating the cell cycle through the tumour suppressor gene p53. There have been several other hints in the literature, that growth hormone not in the pituitary, but actually manufactured in peripheral tissue plays a role in controlling the cell cycle. So, growth hormone is not necessarily only a pituitary hormone. This non-pituitary growth hormone, as originally hypothesised by Michael Waters in Australia, controls the cell cycle, and the less growth hormone in those tissues, the more protected the cell is from proliferation, cancer and the ravages of aging. Non-pituitary growth hormone acting in an autocrine and paracrine fashion appears to regulate the cell cycle, by unleashing mechanisms within the cell that normally restrain growth.

Based on our results we postulate, and it's purely a hypothesis, that if you block growth hormone receptor signalling, as you age, you may be protected from developing cancer. I'll be presenting our work in animal and human models on non-pituitary growth hormone focusing on its potential aging effects. Understanding mechanisms of aging and blocking adverse proliferative mechanisms may be protective.

What are you most proud of in your career so far?
I'm most proud of the fact that I have had so many wonderful, talented fellows and trainees who've gone on to wonderful careers in endocrinology, pituitary in particular. That's my most personally fulfilling professional achievement, I've had the privilege to work with such smart individuals and have watched their careers grow, be nurtured and flourish.

What else are you looking forward to at ECE 2022 this year?
I'm really looking forward to interacting with colleagues and to have the one-on-one conversations that are important for us as individuals, as well as for continuing the scientific dialogue. The opportunity to engage in scientific discourse with each other in a face to face manner is really what I'm looking forward to most.

What do you think are the biggest challenge in your field?
One major challenge is that it's very hard to attract young people to study the pituitary. Diabetes and obesity are much more important as public health issues, so many endocrinologists are engaged in clinical care and research of diabetes, obesity and metabolism.

Another challenge is more technical. As the pituitary is a very small gland, it is very, very difficult to get tissue to study human pituitary cell pathology and physiology. We don't biopsy the pituitary and we don't have access to live, normal pituitary cells. That's why my lab is now focusing on creating induced pluripotent stem cells (iPSCs), which manufacture human pituitary hormones. They are very challenging to develop and maintain but they work, and may help us overcome the lack of human pituitary tissue.

What do you think might be the next big breakthrough in your field?
The availability of induced pluripotent human pituitary cells, which synthesise pituitary hormones with fidelity is going to be a huge advantage.

Another breakthrough is a medical treatment for Cushing's disease. It is probably the most serious pituitary disorder that we treat, with high morbidity and relatively high mortality for patients, who are not well controlled. Cushing's disease remains a very challenging and resistant disorder in pituitary medicine and I think that's the next big frontier for discovery.

What do you enjoy most about your work?
Well, I think that we're very privileged in pituitary medicine that we can offer most of our patients a good life. We offer them quality of life. We don't deal with acute life and death like some other areas of medicine. Very few of our patients harbour malignancies or terminal illness. For the majority of our patients, we offer them a significantly improved quality of life, fewer co-morbidities, with better fertility, self-awareness of their condition, lower anxiety levels, better employment opportunities and less burden on the healthcare system overall.

Why should trainees choose endocrinology, and the pituitary in particular?
Endocrinology is a discipline of systems, all about how cells communicate with each other, both normally and abnormally. Understanding the inter- and intra- cell conversation is really the science of endocrinology. And that is why it’s so fascinating!

The old adage, that the pituitary is the master gland, the conductor of the orchestra, is still true. It's very small and most people haven't heard of it, but the pituitary gland is very important because it maintains cellular homeostasis of every tissue in the body. If I was sent to a desert island and could take just one drug, it would be ACTH. We can't survive for long without this pituitary hormone that controls cortisol production. That is why pituitary medicine is so interesting and important to understand.