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Brain Medicine

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INNOVATORS & IDEAS: RESEARCH LEADER

Hermona Soreq: Revolutionizing neuroscience by elucidating the roles of poly(A) tails, mRNA stability, and acetylcholine in brain-body communication throughout the lifespan

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Hermona Soreq, PhD, holds the Endowed Slesinger Professorship of Molecular Neuroscience at the Hebrew University of Jerusalem. She is an internationally recognized molecular neuroscientist known for her research into the cholinergic system and the small RNA regulators driving the parasympathetic system in men and women under daily and acute stress responses and neurodegenerative diseases like Alzheimer's and Parkinson's diseases (AD, PD). Her studies have long been focused on the roles of acetylcholine in the mammalian nervous system. In the 1980s, Professor Soreq and coworkers cloned the human cholinesterase genes, identified several disease-related mutations and single nucleotide polymorphisms (SNPs) that may impair their functions, and described the unusual features these mutations conferred on carriers under acute stress, exposure to anticholinesterase poisons and diverse disease conditions, including but not limited to myasthenia gravis, ischemic stroke, schizophrenia, bipolar disorder, AD and PD as well as daily stress responses. Soreq further identified microRNA-132 as a principal controller of the cholinergic pathway and studied its impact as well as of other cholinergic-targeted microRNAs as regulators of parasympathetic brain and body functions and neuroinflammation. More recently, she has shifted her interest to the re-discovered transfer RNA fragments (tRFs), and showed that their rapidly declined control over cholinergic transcripts may lead to the fast cognitive deterioration of women living with AD; that they are prominently altered in PD patients' biofluids and that their levels are sex-relatedly modified in the blood of newborn babies, dependent on pre-delivery stress. Her multi-leveled interests in the stress and sex-related cholinergic aspects of AD, PD, adult, and pre-delivery trauma further reflect the impact on acute stress responses as the kernel of the neuroscience research in the current Israeli landscape and has further enabled her a wide-angle view of diverse cholinergic-regulated states and diseases. We are delighted that Professor Soreq answered the Genomic Press Interview, generously sharing her life's trajectory with our readers.

Figure 1. Hermona Soreq, PhD, The Hebrew University of Jerusalem, Israel.

Part 1: Hermona Soreq – Life and Career

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?

I grew up in a small town in Israel, and my high school science teacher told me that he was confident that I would become a scientist and sent me to a summer school at The Hebrew University, where I was indeed hooked to the charms of research and to which I returned after my postdoctoral training at the Darnell lab in the Rockefeller University and several years at the Weizmann Institute. I recall with fondness that 29 years ago, I published a paper in the inaugural volume of *Molecular Psychiatry*. At the time, I was intrigued by Julio Licinio's vision for that journal. It's now exciting to witness that same visionary spirit expand into Genomic Press and its new publication, *Brain Medicine*.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

I was attracted to the cholinergic system early on and got funding to clone the two cholinesterase genes, establish engineered transgenic mice overexpressing them, and test their persistence under anti-cholinesterase poisoning, which was indeed improved—but those mice were also stupid, which seemed a high price to pay for resilience and brought me to study the psychiatric implications of the cholinergic network.

Please share with us what initially piqued your interest in your favorite research or professional focus area.

I liked the story about Otto Loewi and the discovery of acetylcholine. I was then charmed by the concept of microRNAs, which later led me to focus on transfer RNA fragments as regulators of cholinergic functioning.

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What impact do you hope to achieve in your field by focusing on specific research topics?
Others look up to me in my field of expertise, and I am well cited and frequently invited to lecture about my work. On reflection, I must acknowledge the profound impact of the late Edmond and Lily Safra, who established our Brain Research Center. Their vision and support have been instrumental in advancing our work and creating an environment where groundbreaking research can flourish. Their contribution to the field of neuroscience through their generous support cannot be overstated.

Please tell us more about your current scholarly focal points within your chosen field of science.
I am fascinated by the concept of multi-leveled regulation of molecular brain activities and seek to understand it in terms of mental and neurodegenerative diseases.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?
I always look for new surprises and believe that Nature makes no mistakes, so anything we discover has a meaning—often of a regulatory nature.

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that deeply stirs your passions?
My late father taught me that everything is linked to everything else and introduced me to mystery books as a child; I guess that ever since then, I have loved mystery stories and sought new links between the mechanisms of action that make our brains work the way they do.

What do you most enjoy in your capacity as an academic or research leader?
Going to work has become a relief from the burdens of everyday stresses, which are genuinely very heavy these days. So, work is my refuge from war.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?
I love reading and like this activity as my leisure time—it also assists in escaping the harsh reality around us this past year. I also like cooking for my family, which is close to biochemistry in my mind—many years ago, there was a short article in Science on the biochemistry of meringue that I will never forget. I also enjoy traveling, and science gives me ample opportunities to do that.

Part 2: Hermona Soreq – Selected questions from the Proust Questionnaire[1]

What is your idea of perfect happiness?
Peace and interaction with other peace-seeking individuals.

What is your greatest fear?
After October 7th, 2023—that it happens again.

Which living person do you most admire?
Jean Pierre Changeux, who is the man of all virtues and masters both science, arts and humanities.

What is your greatest extravagance?
A little while ago, my 12-year-old granddaughter and several of her girlfriends visited my lab and learned some of what we do—and one of them told me, "You are a truly enchanting woman!" which was really great.

What are you most proud of?
At work- my ex-graduates who succeed in their scientific journeys, current students and postdocs who are the best there are and students who ask smart questions at lectures.

What is your greatest regret?
Failure to transfer the love of research to some of my trainees and students who think that it is too demanding.

What is the quality you most admire in people?
Curiosity and the ability to take it to higher levels of understanding.

What is the trait you most dislike in people?
Dishonesty and disrespect to others.

What do you consider the most overrated virtue?
Success in one's career, which depends on much more than personal merits.

What is your favorite occupation (or activity)?
Reading novels.

Where would you most like to live?
Where I do: a small 3,000-years-old village in the outskirts of Jerusalem.

What is your most treasured possession?
An antique coin from the ancient kingdom of Jerusalem, 2000 years ago.

When and where were you happiest? And why were so happy then?
When my eldest son was born and a new life began.

What is your current state of mind?
Scared of the threats of worldwide war in the air.

What is your most marked characteristic?
My friends say that I am hopelessly optimistic, but I fear that I am losing that virtue.

Among your talents, which one(s) give(s) you a competitive edge?
The capacity to link solutions to emerging research questions and come up with answers.

What do you consider your greatest achievement?
Cloning of the two human cholinesterase genes before the human genome project.

If you could change one thing about yourself, what would it be?
Lose weight.

What do you most value in your friends?
Their friendship and independent personalities.

Who are your favorite writers?
I would have to say Lev (Leo) Tolstoy—his books just have this way of getting under your skin and making you see the world differently, you know? Like in *War and Peace*, he captures these huge historical events but also dives deep into the characters' inner lives.

[1] In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35-question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust's handwritten answers were auctioned off for $130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.

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Who are your heroes of fiction?
Recently, I was captivated by Andrew Bevel from Hernan Diaz's novel *Trust*—or *Spaces* as it is called in the Hebrew translation I read. Have you come across it? Bevel isn't your typical hero, but that is what makes him so fascinating. He is this wealthy financier in 1920s New York, who made his biggest killing by anticipating and "shorting" the financial collapse of 1929. The way Diaz peels back the layers of his character through different perspectives is just... wow! It really makes you question the nature of truth and power.

Who are your heroes in real life?
John Gurdon, Eric Kandel, Jean Pierre Changeux.

What aphorism or motto best encapsulates your life philosophy?
The wheat will grow again...

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