BIOGRAPHICAL SKETCH

NAME:**Asya Rolls, PhD**

eRA COMMONS USER NAME: **ROLLS.ASYA.**

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POSITION TITLE: **Professor**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date	Completion Date	FIELD OF STUDY
Stanford University, CA	Postdoc	10/2008	10/2012	Psychiatry
Weizmann Institute of Science, Israel	Postdoc	10/2007	08/2008	Neuroimmunology
Weizmann Institute of Science, Israel	PhD	05/2002	09/2007	Neuroimmunology
Technion, Israel	MSc	10/1999	10/2001	Molecular biology
Technion, Israel	BSc	10/1995	08/1999	Life sciences

A. Personal Statement

The philosophical mind-body problem examines the relationship between the mind, a mental process, and its impact on the body, a physical entity. Such interactions are manifested in modern medicine by the emergence of disease following stress or recovery in response to placebo treatment. Yet, the underlying physiological principles remain elusive. My research group investigates this question by examining the brain's interaction with the immune system—our primary defense. We are exploring how the brain reacts to immune challenges and how emotional and cognitive brain functions affect immunity. Our goal is to unravel the physiological underpinnings of this interaction to, on the one hand, understand the genesis of psychosomatic disorders triggered by emotional processes and, on the other, harness the body's endogenous restorative capacity.

Ongoing and recently completed projects that I would like to highlight include:

2017-2022
International Research Scholar
Howard Hughes Medical Institute (HHMI)-Wellcome trust

2017-2022
ERC starting grant
Neuronal regulation of immunity, Rolls (P.I).

2023-2028
ERC consolidator grant
Neuronal regulation of the fascia, Rolls (P.I)

B. Positions, Scientific Appointments and Honors

Positions:

2008 – 2012 Postdoctoral fellow, Department of Psychiatry, Stanford University, CA
2012 – 2018 Assistant Professor, Faculty of Medicine, Technion, Israel
2018 – 2022 Associate Professor, Faculty of Medicine, Technion, Israel
2022- present Full Professor, Faculty of Medicine, Technion, Israel

Honors:

2008 Esther Hellinger Memorial Prize (Weizmann Institute of Science)
2008 Fulbright Post-Doctoral Fellowships (US Government)
2008 Rothschild postdoctoral fellowship

2009 ERA-Net NEURON- Excellent Paper in Neuroscience award
2009 Weizmann Institute Award for Women in Science
2009 EMBO long-term fellowship
2011 Most Notable Publications in Sleep 2011 (Sleep Research Society)
2011 NARSAD Young Investigator Award
2014 TSA Theeman Scholar (Australian Technion Society)
2014 FENS-Kavli network of Excellence- elected member (until -2017)
2017 Krill Prize for excellence in scientific research (Wolf Foundation)
2017 Adelis Brain Research Award
2017 Howard Hughes Medical Institute (HHMI)-Wellcome - International Research Scholar
2018 Member of the Israeli Young Academy of Science and Humanities
2018 Member of the International Advisory Board of the International Society of Neuroimmunology (until 2023)
2019 Rappaport Prize for Young and Promising Scientists
2021 The Diane Sherman Prize for Medical Innovation for a Better World
2022 Juludan Research Prize
2023 The Weizmann Prize for Science

C. Contributions to Science

i) Discovered that the brain's reward system activity boosts antibacterial and anti-tumor immunity. Positive expectations contribute to the clinical benefits of the placebo effect. Such positive expectations are mediated by the brain's reward system; however, it remains unknown whether and how reward system activation affects the body's physiology and, specifically, immunity. We showed using chemogenetics that activation of the ventral tegmental area (VTA), a key component of the reward system, strengthens immunological host defense. We demonstrated these effects in the context of antibacterial and anti-tumor immunity. Mechanistically, by chemically ablating the sympathetic nervous system (SNS), we showed that the reward system's effects on immunity are, at least partly, mediated by the SNS. This pioneering approach of applying chemogenetic techniques to establish the causal effects of specific brain activity on immunity introduced new avenues for understanding how emotions and cognition can modulate immune responses, illuminating some of the physiological processes underlying the placebo effect.

1. Ben-Shaanan TL, Azulay-Debby H, Dubovik T, Starosvetsky E, Korin B, Schiller M, Green NL, Admon Y, Hakim F, Shen-Orr SS*, Rolls A*. Activation of the reward system boosts innate and adaptive immunity. *Nature Med*. 2016 Aug;22(8):940-4. doi: 10.1038/nm.4133. PubMed PMID: 27376577.

2. Ben-Shaanan TL, Schiller M, Azulay-Debby H, Korin B, Boshnak N, Koren T, Krot M, Shakya J, Rahat MA, Hakim F, Rolls A. Modulation of anti-tumor immunity by the brain's reward system. *Nature Commun*. 2018 Jul 13;9(1):2723. doi: 10.1038/s41467 -018-05283-5 PubMed PMID: 30006573

3. Ben-Shaanan T, Schiller M, Rolls A. Studying brain-regulation of immunity with optogenetics and chemogenetics; A new experimental platform. *Brain Behav Immun*. 2017 Oct;65:1-8. doi: 10.1016/j.bbi.2016.11.024. Epub 2016 Nov 24. Review. PubMed PMID: 27890661.

4. Schiller M, Ben-Shaanan TL, Rolls A. Neuronal regulation of immunity: why, how and where? *Nat Rev Immunol*. 2020 Aug 18. doi: 10.1038/s41577-020-0387-1.

ii) Characterized the dynamic changes in the brain's immune compartment in different physiological conditions. The brain and its borders create a highly dynamic microenvironment populated with immune cells that are either brain residents or temporally infiltrate from peripheral blood. We showed, using high dimensional characterization with CyTOF, mass cytometry, that the composition of the brain immune compartment varies even in naïve mice. By comparing immune cell profiles between the brain and blood, we could characterize previously undescribed cell subsets of CD8 T cells, B cells, NK cells, and dendritic cells in the naive brain and identify CD44 as a marker for infiltrating immune populations. Moreover, we found that the immune composition of the brain is affected by the physiological state, and even short-term sleep deprivation could increase the abundance of B cells in the brain compartment. These findings demonstrated the peripheral effects on the brain's immune compartment and

offered a new insight into how sleep disorders can affect brain function and potentially contribute to neurodegeneration and neuroinflammation.

1. Korin B, Ben-Shaanan TL, Schiller M, Dubovik T, Azulay-Debby H, Boshnak NT, Koren T, Rolls. High-dimensional, single-cell characterization of the brain's immune compartment. *Nature Neurosci*. 2017 Sep;20(9):1300-1309. doi: 10.1038/nn.4610. PubMed PMID: 28758994.

2. Korin B., Dubovik T., Rolls A. Mass cytometry analysis of immune cells in the brain. *Nature Protoc*. 2018 Feb;13(2):377-391. doi: 10.1038/nprot.2017.155. Epub 2018 Jan 25. PubMed PMID: 29370157.

3. Korin B, Avraham S, Azulay-Debby H, Farfara D, Hakim F, Rolls A. Short-term sleep deprivation in mice induces B cell migration to the brain compartment. *Sleep* 2019 Sep 25 doi.org/10.1093/sleep/zsz222

iii) Sympathetic nervous system (SNS) locally controls the endothelial gateway of immune cells to the tissues. The SNS is composed of an endocrine arm, regulating blood adrenaline and noradrenaline, and a local arm, a network of fibers innervating immune organs. We found that the local arm of the SNS can regulate an inflammatory response in the colon. We used optogenetics to locally activate sympathetic fibers in the colon and found that in contrast to systemic application of noradrenaline, local activation of sympathetic fibers decreased endothelial expression of the adhesion molecule MAdCAM-1, reducing immune cell infiltration and colitis-induced inflammation. Thus, we found that the local sympathetic fibers engage in unique control of the endothelial gateway between the circulation and the tissue. This finding also offers a new potential mechanism whereby the brain can induce precise spatial and temporal control over the peripheral immune system.

1. Schiller M., Azulay-Debby H., Bushnak N., Ben Shannan T., Korin B., Koren T., Krot M., Elyahu Y., Hakim F., Rolls A. Optogenetic activation of local colonic sympathetic innervations attenuates colitis by limiting immune cell extravasation. *Immunity* 2021 DOI:https://doi.org/10.1016/j.immuni.2021.04.007

iv) Demonstrating the existence of neuronal traces of "immunological memories" in the brain. To define the systemic neuroimmune interactions in health and disease, we recently suggested immunoception as a term that refers to the existence of bidirectional functional loops between the brain and the immune system. This concept suggests that the brain constantly monitors changes in immune activity and, in turn, can regulate the immune system to generate a physiologically synchronized response. Therefore, the brain has to represent information regarding the state of the immune system, which can occure in multiple ways. One such representation is an immunengram, a trace that is partially stored by neurons and partially by the local tissue.

1. Koren T., Yifa R., Amer M., Krot M., Boshnak N., Ben-Shaanan TL., Azulay-Debby H., Zalayat I., Avishai E., Hajjo H, Schiller M., Haykin H., Korin B., Farfara D., Hakim F., Kobiler O., Rosenblum K., and Rolls A., Insular Cortex Neurons Encode and Retrieve Specific Immune Responses, *Cell* 2021. doi: 10.1016/j.cell.2021.10.013

2. Koren T. Rolls A. Immunoception: defining brain regulated immunity. *Neuron* 2022; 220(21); 3425-3428; doi: 10.1016/j.neuron.2022.10.016.PMID: 36327893

3. Rolls A. Immunoception: the insular cortex perspective. *Cell Mol Immunol*. 2023 Nov;20(11):1270-1276. doi: 10.1038/s41423-023-01051-8. PMID: 37386172