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From the Desk of the Editor-in-Chief: Excerpts from the Society for Neurochemistry (ESN) Future Perspectives for European Neurochemistry Highlighting the Symposium Asking "Autism, Epilepsy, Intellectual Disability Where Do These All Meet?"

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Focusing on pathologies that unite different brain diseases and employing cutting-edge technologies was the basis of a recent virtual symposium entitled "Autism, Epilepsy, Intellectual Disability Where Do These All Meet?" This symposium joined five other excellent symposia constituting the European Society for Neurochemistry (ESN) First Virtual Conference held in May 2021. Please refer to the overview by Eva-Maria Blumrich and Sara Grassi, in this special issue of the Journal of Molecular Neuroscience, for a detailed description of the meeting and the featured articles.

The topic raised by the autism/intellectual disability/epilepsy symposium joins our previous Virtual ESN Mini-Conference in conjunction with the FENS Forum 2020 entitled "Molecular Mechanisms of Cognitive Impairment and Intellectual Disability" (Gozes et al. 2020). Now, with young investigators, representing the best of Israel's young investigators, the subject was revisited and expanded. Chaired by Moshe Giladi and Daniel Bar, Moshe Giladi first discussed the structural basis of heterotetrameric assembly and disease mutations in the human cis Prenyltransferase (h cis PT) complex, recently published in Science Advances (Giladi et al. 2022) and in Nature Communications (Bar-El et al. 2020). This research joins another interesting Elife article by the same group entitled "Two de novo GluN2B mutations affect multiple NMDAR-functions and instigate severe pediatric encephalopathy" (Kellner et al. 2021). Together, these findings are in agreement with the concept of similar mechanisms uniting different brain diseases (Gozes 2021, Bahrami et al. 2022).

The lecture of Moshe Giladi was followed by a Lecture by Gidon Karmon (then MD/PhD student in my laboratory, now, PhD approved). His lecture was entitled "Lessons from a novel genome-edited mouse for the autism intellectual disability activity-dependent neuroprotective protein (ADNP) syndrome." Our paper describing novel genome-edited ADNP syndrome mice that exhibit dramatic sex-specific peripheral gene expression with brain synaptic and Tau pathologies, is now published (Karmon et al. 2022). This study boasts an international collaboration with leading laboratories in Israel, Canada, Germany, and the Czech Republic. The paper was chosen by the Editor of Biological Psychiatry to be highlighted in an excellent Commentary by Haitham Amal, emphasizing sex and the brain and focusing on the protective effects of the ADNP fragment, drug candidate NAP (davunetide) in the novel ADNP syndrome model (Amal 2022). This drug candidate, discovered in our laboratory (Bassan et al. 1999; Gozes 2020) and now licensed for clinical development to ATED Therapeutics Ltd., was recently shown to include an SH3-binding site interacting with the SHANK3 SH3-domain and providing protection in an additional autism model of SHANK3 mutation (modeling the Phelan McDermid syndrome) (Ivashko-Pachima et al. 2022). With SHANK3 also presenting schizophrenia-causing mutations, these studies ignite interest from a basic and from a clinical development perspective.

For the electrophysiological aspects, we partnered with Moran Rubinstein (Karmon et al. 2022), whose student Shir Quinn presented the functional analysis of the developmental delay caused by SCN8A G1625R mutation. This lecture investigated aberrant brain development coupling with epilepsy. In this respect, a recent paper led by Moran Rubinstein including Shir Quinn, published in Epilepsia was entitled:

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"Convulsive seizures and some behavioral comorbidities are uncoupled in the Scn1aA1783V Dravet syndrome mouse model" (Fadila et al. 2020).

Haitham Amal closed the session focusing on the role of nitric oxide (NO) in autism, which was also featured in the Journal of Molecular Neuroscience (Hamoudi et al. 2021) and more recently in an article tying arsenic altering nitric oxide signaling similar to autism spectrum disorder and Alzheimer's disease-associated mutations (Tripathi et al. 2022). Furthermore, a proteomics study by the Amal group revealed common alterations in mTOR signaling pathway in autism and Alzheimer's disease mouse models (Mencer et al., 2021). These interesting findings linking delayed/atypical nervous system development to accelerated/neurodegenerative aging were also noted in our papers discovering somatic autism/intellectual disability gene mutations in Alzheimer's disease postmortem brains (Ivashko-Pachima et al. 2021), Alzheimer's—like tauopathy in the young autistic brain (Grigg et al. 2020) and co-regulation of ADNP and healthy aging-associated proteins like SIRT1 (Hadar et al. 2021) and FOXO3 (Karmon et al. 2022). All of these pave the path to a better understanding of brain diseases and future disease management by employing molecular neuroscience and neurochemistry at their best.

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Declarations

Conflict of Interest I am a Founder, Chief Scientific Officer of ATED Therapeutics LTD, developing NAP (Davunetide) first for the ADNP syndrome, under patent protection.

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