A novel differentiation protocol to obtain functional 3D human neural culture model

D'Aloia A.[1], Blasa S.[1], Lorenzin S.[1], Pastori V.[1], Ceriani M.[1,2] and Lecchi M[1]. and Costa B[1].

E-mail: alessia.daloia@unimib.it

[1] Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy

[2] Milan Center for Neuroscience (NeuroMI), University of Milano-Bicocca, Piazza dell'Ateneo Nuovo 1, 20126 Milano, Italy

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Abstract: This project aimed to employ and validate a new three-dimensional in vitro model of functional human neurons that could be used to study Alzheimer's disease (AD), which is the most common late-onset and progressive neurodegenerative disorder, characterized by progressive dementia. At present, no therapies in clinical use can effectively impact the disease course. To complicate drug discovery in AD, there are dozens of models available, including many mouse models and cell lines that have been altered to express some of the genes known to cause the disease in humans. But these models fail to mimic critical aspects of the disease that occur in patients, and this may be the reason why molecules effective in pre-clinical studies fail in humans.

To develop a pathological model is required a specimen able to represent the brain's physiological environment, including differentiated neurons and microglia. For this reason, the human neuroblastoma cellular line SH-SY5Y was chosen, and treated with an innovative differentiation protocol. This procedure is protected by secret and it consists of 7 days of pre-differentiation in a pre-differentiation medium, followed by differentiation with an appropriate medium for 40 days. The whole differentiation process occurs in a matrix, allowing the development of a 3D culture and recreating a cerebral environment more similar to the physiological one. Thanks to this innovative protocol, we obtained mature cholinergic neurons with spontaneous electrical activity.