Titre de l'annonce	PhD position in neuroscience
3 mots clé -	high-content screening; microfluidics; microelectrode arrays
Ville	Lille
Pays	France
Texte de l'offre	A PhD student position will be available in the team of Jean-Charles Lambert at the Institut Pasteur de Lille with the details below. Potential applicants should contact Devrim Kilinc at mailto:devrim.kilinc@pasteur-lille.fr with their CV, cover letter, and contact information of two or more academic references. Project title: Screening Alzheimer's genetic risk factors against amyloid synaptotoxicity Project description: Genome-wide association studies reported over 200 genetic risk factors for Alzheimer's disease (AD); however, their putative roles in synapse maintenance are not fully understood (doi: 10.1007/s00401-019-02004-0 and doi: 10.1038/s41588-019-0358-2). Considering that synapse loss is an early event in the AD process, dissecting the pre- and postsynaptic mechanisms in which AD risk genes are involved may lead to novel therapeutic targets. Our microfluidic co-culture model enables gene expression exclusively in pre- and postsynaptic neurons and exposes synapses to A peptides secreted from cell lines expressing wild-type or mutant (V717I) APP (doi: 10.1093/braincomms/fcaa139). We extended this model into a medium-throughput screening device, which packs 48 co-cultures into standard multi-well plate footprint, thereby allowing automated microscopy. We are currently screening all AD risk genes expressed in the brain for their impact on synaptic connectivity in 384-well plates. The objective of this project is to further screen risk genes for their capacity to block amyloid-β (Aβ)-induced synaptotoxicity and to characterize identified mechanisms via electrophysiology. To this end, we will (i) screen top 20% AD risk genes whose silencing

	is detrimental to synapses, by overexpressing them in pre- or postsynaptic neurons cultured in the medium-throughput device; (ii) validate protective mechanisms via high-resolution confocal microscopy and by chemically inhibiting the gene product whenever possible; and (iii) further characterize validated genes in microfluidic co-culture devices coupled to microelectrode arrays (MEAs) through the induction of synaptic potentiation in postsynaptic neurons upon high-frequency stimulation of presynaptic neurons. Protective mechanisms identified will be considered for future therapies. Keywords: primary neurons; microfluidic devices; high-content screening; micro-electrode arrays; genetic risk factors Profile and skills required: The candidate should have a solid background in cell biology, biochemistry, or a related field and a keen interest in neurobiology/neurodegenerative diseases. Academic achievements as evidenced by class ranking, fellowships, and awards are sought after. Hands-on experience in in vitro cell biology and fluorescent microscopy are desirable, but not required. Candidates are expected to work in a dynamic and collegial environment that requires strong organizational and communication skills.
Date de fin de publication :	16/04/2021
Type d'emploi	Thèse – PhD
Type de contrat	Concours pour un contrat doctoral (regional co-financement requested)
Date limite de candidature	**23/04/2021**
Date début de fonction	01/10/2021

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