

<b>PI</b>	<i>Lodato Simona</i>
<b>PROJECT TITLE</b>	<i>Investigating cortical circuit assembly and dysfunction in human 3D cortical organoids</i>
<b>ABSTRACT</b>	<p>During cerebral cortex development, GABAergic interneurons (INs) recognize and pair - in a subtype-specific manner<sup>1</sup> - with excitatory projection neurons (PNs) to ensure the fine excitatory-inhibitory (E/I) balance essential for proper circuit function<sup>2</sup>. Although E/I alterations are often associated with the onset of developmental and epileptic encephalopathies (DEE), the underlying precise cellular, molecular and functional events are still elusive. Animal models, albeit instrumental, present limitations due to the inherent differences in brain development and function. We will exploit human 3Dcortical organoids<sup>3</sup> from DEE patient-specific iPSC to investigate the cellular interplay between PNs and INs<sup>4</sup>. Integrating molecular (scRNA seq and Tissue Imaging Mass spectrometry) and functional (Calcium Imaging/MEA) analysis, we aim at dissecting pathological mechanisms affecting E/I microcircuits assembly (linked to the recurrent seizures) to identifying new substrates for therapeutic solutions.</p>
<b>FUNDING REFERENCE (AMOUNT, STARTING DATE AND DURATION)</b>	<p>Ministero della Salute Ricerca Finalizzata Giovani Ricercatori  GR-2019-12368561  450,000 Euros  Anticipated Project Start Date: Spring-Summer 2021  (Agreement signed on February 2021)  Duration: 36 months</p>
<b>MAIN TECHNICAL APPROACHES TO CARRY OUT THE PRESENT PROJECT</b>	<ul style="list-style-type: none"> <li>- Cell culture experience</li> <li>- Molecular biology techniques for cloning, transfection and transduction strategies</li> </ul>
<b>SCIENTIFIC REFERENCES RELATED TO THE PRESENT PROJECT</b>	<p><sup>1</sup>Lodato et al., Excitatory projection neuron subtypes control the distribution of local inhibitory interneurons in the cerebral cortex, <b>Neuron</b>, 2011; doi: 10.1016/j.neuron.2011.01.015.</p> <p><sup>2</sup>Lodato and Arlotta, Generating neuronal diversity in the mammalian cerebral cortex, <b>Annual Review of Cellular and Developmental Biology</b>, 2015; doi: 10.1146/annurev-cellbio-100814-125353</p> <p><sup>3</sup>Tambalo and Lodato, Brain organoids: Human 3D models to investigate neuronal circuits assembly, function and dysfunction, <b>Brain Research</b>, 2020; doi: 10.1016/j.brainres.2020.147028</p> <p><sup>4</sup>Sloan et al., Generation and assembly of human brain region-specific three-dimensional cultures, <b>Nature Protocol</b>, 2018; doi: 10.1038/s41596-018-0032-7.</p>