***DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO***

**41° Ciclo**

**Title of the research:** Neuronal response to space stress: study of the effect of chronic expposure to ionizing radiation and altered gravity in terms of protein quality control and aggregation in a human neuroblastoma cell model

**Supervisor:** Dr. Giuseppe Esposito (giuseppe.esposito@iss.it)
**Co-supervisors:** Dr. Niccolò Candelise; Dr. Marcello Belfiore
**Tutor:** Ada Maria Tata (adamaria.tata@uniroma1.it)

**Host Institution:** Italian National Institute of Health (Istituto Superiore di Sanità, ISS)

**Summary**
Space exploration is one of the major scientific human achievements. Astronauts are however exposed to extreme stressful conditions, such as altered gravity and ionizing radiation. These factors are known to strongly impact the nervous system, leading to cognitive damage. However, little is known on the effects induced by these stressors on neurons' protein quality control machinery, whose derangement can lead to protein aggregation similar to what is observed in post-mortem patients affected by neurodegenerative diseases (e.g., Alzheimer's Disease, Parkinson's Disease).The present proposal aims to study the effect of the main space stressors, i.e., high and low LET ionizing radiation and altered gravity, in a cellular model of human neuroblastoma differentiated into post-mitotic neurons. The project aims to specifically identify alterations in the protein quality control machinery and the eventual misfolding and aggregation into amyloids following chronic exposure to stressors. Human neuroblastoma SH-SY5Y cells will be employed and differentiated into mature neurons by the application of Retinoic Acid and Brain Derived Neurotrophic Factor. Both the direct effect and the indirec effect (the bystander effect) will be evaluated in terms of cell viability, protein expression and amyloid burden. Altered gravity will be investigfated using a clinostat, which coud further produce three-dimensional SH-SY5Y spheroids and potentially brain organoids by induction of differentiation during the rotation.