Bando della Ricerca Finalizzata 2019											
TITOLO PROGETTO	**CODICE PROGETTO**	**CUP**	**RUOLO**	**TIPOLOGIA PROGETTUALE**	**RESPONSABILE SCIENTIFICO**	**QUOTA IRCCS**	**DATA INIZIO**	**DATA FINE**	**ENTE CAPOFILA**	**TEMATICA PRINCIPALE**	**ABSTRACT**
Dysfunction of RNA processing and autophagy in human ALS disease cell models: a bioassay for new therapeutic strategies	RF-2019-12368778	F25F19000300001	Partner	Progetti ordinari di ricerca finalizzata (RF): Theory-enhancing	**Francesco Fornai**	110.000,00 €	01/06/2021	31/05/2025	Istituto Auxologico Italiano	Neurologia e Psichiatria	ALS is a fatal neurodegenerative disease that is often associated with mutations in TARDBP (TDP-43) and C9ORF72 genes, which are involved in RNA metabolism and protein-quality control systems, including autophagy. FTD has a similar pathogenetic mechanism. Cytoplasmic aggregates of TDP-43 represent a neuropathological hallmark of ALS and FTD, namely TDP-43 proteinopathies. TDP-43 is also recruited into stress granules (SG), RNA/protein complexes formed in response to cellular stress. A failure of SG clearance by autophagy may lead to pathological TDP-43 aggregates, thus promoting ALS/FTD pathogenesis; however, the issue is still under debate. Therefore, our aim is to investigate ALS/FTD- related molecular mechanisms underlying the intersection between SGs, TDP-43 aggregation, and autophagy. As an endpoint, the effects of genetic and pharmacological modulation of autophagy will be tested on TDP-43 pathologic aggregation, aimed at developing new therapeutic strategies for ALS/FTD.