Ministero dell'Istruzione, dell'Università e della Ricerca
Direzione Generale per il Coordinamento, la Promozione e la Valorizzazione della Ricerca
Uff. V.

Rendiconto di spesa Fondi 5 per mille ANNO 2020
Enti della Ricerca Scientifica

Ente[1]: Fondazione Telethon
Codice fiscale: 04879781005
Indirizzo sede legale: Via Varese 16B 00185 Roma
Referenti (De Dilectis Isabella, Tel. 06 44015756, idedilectis@telethon.it)

Attività:

Il 5 per mille relativo all'anno 2020 è stato recepito dalla Fondazione Telethon nel bilancio al momento dell'emissione delle liste definitive dei beneficiari, avvenuta in data 08/06/2021, quindi attribuito per competenza nel bilancio 2021. L'erogazione dell'importo spettante, pari a € 2.531.741,58 è avvenuta in data 30/11/2021.

Coerentemente con le regole di rendicontazione, l'importo del cinque per mille in oggetto è stato utilizzato per la copertura di oneri ammissibili, sostenuti nel corso del periodo di riferimento, dalla data uscita elenchi (08/06/2021) alla data di incasso più 12 mesi (30/11/2022).

Il criterio di formazione delle poste, conformemente al bilancio di esercizio della Fondazione Telethon, risponde al principio di competenza, e gli importi esposti in questa sede, opportunamente aggregati, sono parte integrante dei bilanci stessi.

Il contributo del ministero è stato utilizzato per cofinanziare progetti di ricerca aventi ad oggetto malattie genetiche rare. Essi sono stati selezionati tramite il bando generale Telethon da una commissione internazionale nell'ambito di una attenta analisi delle potenzialità progettuali. I progetti selezionati, oggetto di rendicontazione sono tutti del tipo "gestione diretta".

I progetti di ricerca finanziati sono dedicati a varie tipologie di malattie genetiche che includono malattie neurologiche, malattie metaboliche, malattie del sangue, malformazioni congenite e malattie oftalmiche. Ogni progetto, a sua volta, si occupa di uno o più aspetti della ricerca, partendo dalla ricerca di base per studiare i meccanismi che portano all'insorgere della malattia, sino ad arrivare a possibili approcci terapeutici. Di seguito a titolo esemplificativo alcune progettualità.

Malattie neurologiche. I progetti riguardano studi su malattie neurologiche che causano diverse patologie quali: disabilità intellettive come, ad esempio, la sindrome di Rett, epilessie come la

[1] Istituzione beneficiaria del contributo del 5 per mille.

sindrome di, atassie che provocano *difficoltà nell'eseguire movimenti volontari quali l'*Atassia parossistica familiare.

Malattie metaboliche. I progetti che studiano malattie mitocondriali cioè causate da un difetto nel funzionamento dei mitocondri, gli organelli che producono energia necessaria alle nostre cellule per funzionare. Le malattie studiate causano numerosi effetti patologici quali convulsioni, epilessie, debolezza muscolare e problemi cardiaci. I ricercatori in questi casi studiano da una parte i meccanismi molecolari coinvolti nell'insorgenza di queste patologie e dall'altra verificano l'efficacia di potenziali nuovi farmaci in modelli animali.

Malattie del sangue. Un progetto è dedicato all'emofilia di tipo A grave, in cui un fattore della coagulazione difettoso (fattore VIII) causa emorragie spontanee e prolungate. I ricercatori si propongono di studiare a fondo il ruolo del fattore VIII proponendo anche un possibile approccio terapeutico mediante terapia genica.

Malformazioni congenite. Un progetto sulla sindrome da delezione 22q11.2, un'aberrazione cromosomica che causa diversi effetti patologici quali dismorfismi facciali, anomalie del palato, ritardo dello sviluppo, malattie cardiache e immunologiche. Il progetto si propone di investigare in un modello animale i possibili effetti positivi di un trattamento con ossitocina, un ormone naturale, sui deficit sociali, cognitivi e del sistema immunitario che caratterizzano la sindrome.

Malattie oftalmiche. Un progetto sulla retinite pigmentosa, una malattia che causa degenerazione della retina e porta a una progressiva riduzione della vista e in alcuni casi anche a cecità. L'obiettivo di questo progetto è lo sviluppo di un trattamento farmacologico utilizzando piccole molecole proteiche sintetiche potenzialmente in grado di proteggere la retina dagli effetti degenerativi delle mutazioni.

Nel periodo di riferimento i progetti finanziati con le risorse del 5 per mille sono le seguenti:

Descrizione Progetto	**Commessa**
Telethon Undiagnosed Disease Program - Revised Proposal	GSP15001
Finding pharmacological treatments for Tubular Aggregate Myopathy	GGP19110
Experimental gene therapy in mitochondrial disorders	GGP19007
Autosomal Dominant Osteopetrosis Type 2 (ADO2): close to the cure. What do we miss?	GGP19031
Structural and functional characterization of HERG potassium channels' enhancers as a novel therapeutic strategy for Long QT Syndrome	GGP19134
Identification of druggable pro-resolving mechanisms in Sickle Celle Disease	GGP20116
New insights on the pathogenesis of hereditary Cerebral Cavernous Malformations	GGP19202
Store-Operated Calcium Entry (SOCE): role in skeletal muscle function and disease	GGP19231
Functional dissection of the molecular underpinnings of 7q11.23 syndromes: bridging pathogenic insight to drug discovery at single cell resolution	GGP19226
Regulation of pathogen-specific T-cell responses in patients with Hyper-IgE syndrome (HIES)	GGP19323

Modeling Wolman disease using genetically engineered human liver organoids	GGP20031
Toward gene therapy for Dravet syndrome: uncovering dynamics of reversibility and mechanisms of Scn1a gene modulation	GGP19249
Gene editing in Myotonic Dystrophy type 1: assessment of efficiency, safety and therapeutic effect of CTG-repeat deletion in a mouse model of disease.	GGP19035A
Exploiting regulatory T-cell metabolic reprogramming and vascular tropism as therapeutic tools for Familial Hypercholesterolaemia.	GGP19146
Interaction of PRRT2 with Na+ channels: pathogenetic basis and new targets for the cure of PRRT2- associated paroxysmal disorders	GGP19120
Dissecting new functions of the Nijmegen breakage syndrome gene in cerebellar development	GGP20135
Novel therapeutic approaches for AEC syndrome	GGP20124
Knockdown and Replacement of MFN2: a Gene Therapy to treat Dominantly Inherited Peripheral Neuropathy CMT2A	GGP19002
Plasmalogen-based therapeutic strategy for the treatment of Hereditary Spastic Paraplegia	GGP19304
Optic atrophy 1 dependent signals in retinal ganglion cells: from identification to a therapy for autosomal dominant optic atrophy	GGP19089
A therapeutic approach for rare genodermatoses caused by aberrant connexin hemichannels	GGP19148
Towards Precision Medicine with Human Induced Pluripotent Stem Cells for Dystrophin Associated Cardiomyopathy	GUP19012
Exploiting a bacterial redox cycler against mitochondrial diseases linked to respiratory complex dysfunction	GGP19118
Exploiting whole-brain strategies of gene therapy and novel therapeutic targets in Rett syndrome mouse models	GGP19038
Mechanisms of axonal degeneration in late onset CMT1B neuropathies: molecular pathways and therapeutic approaches	GGP19099
Investigating necroptosis in Autosomal Recessive Juvenile Parkinsonism and potential rescue by pharmacological Kar antagonism	GGP20048
Meninges as an overlooked pharmacological target for Globoid Cell Leukodystrophy	GGP19250
From coagulation to angiogenesis: new roles for FVIII in endothelial functionality	GGP19201
Cell-based therapy for Congenital Thrombotic Thrombocytopenic Purpura	GGP20073
Intracellular chloride dynamics in autistic brain: a better understanding is needed for tailored cures.	GGP19281
Finding new targets to counteract brain progenitor cells dysregulation in AGC1 deficiency hypomyelination: a multi-disciplinary approach.	GGP19067
Joubert syndrome: beyond conventional mendelian genetics	GGP20070
Preclinical efficacy study of PERK signaling inhibitors and TUDCA in Marinesco-Sjögren syndrome	GGP20071
Molecular characterization of disease-linked polynucleotide phosphorylase variants (POLYVAR)	GGP20001
The role of SMN protein in translation: implications for Spinal Muscular Atrophy	GGP19115

Patient-specific molecular mechanisms of Fragile X Syndrome pathogenesis and Fragile-X associated phenotypes	GGP20105
SAP-mediated DGKa inhibition triggers a novel cell fate switch in antigen-activated T cells: implications for XLP1 therapy	GGP16252
Innovative Strategy to Enhance the Efficiency and Safety of Gene Therapy for CDKL5 Deficency Disorder	GGP19045
Cell-Penetrating SIL1 Protein Replacement Therapy for Marinesco-Sjogren Syndrome	GGP20092
Liver-directed promoterless gene targeting without the use of nucleases as a potential therapy for Fabry disease	GGP20128
Metabolism of polysialic acid: new insight into pathological mechanisms and potential treatments for Huntington's disease	GGP20101
Illuminating the biology of the GPR101 receptor: analysis of its transcriptional regulation and validation of new ligands	GGP20130
Elevating spastin by inhibiting its degradation: a possible therapeutic approach in Hereditary Spastic Paraplegia (HSP)	GGP20040
A new RNA-based therapy for the Fragile X Syndrome	GGP20137
Detailing and modeling dendritic spine pruning pathways and cognition in Rab39b XLID mouse model	GGP20065
The Human δ-Globin Gene as a therapeutic tool for β-Hemoglobinopathies. Post GWAS target validation and evaluation of molecules in preclinical models	GGP20046
Spermidine as new candidate for the treatment of COL6 myopathies (SpeCTre-COL6)	GGP19229
Cure MERRF: from fibroblasts to organoids speeding basic science into clinical trials for mitochondrial diseases	GGP20115
Mechanistic dissection of Polycomb-dependent dysregulation in Weaver syndrome neural lineages	GGP19295
MAMA: Molecular Analysis and manipulation of Metabolic signalling in Adenylosuccinase deficiency	GGP20109
In-depth phenotyping and experimental therapy of Cole Carpenter Syndrome	GGP20074
Ribosomal pathologies: mechanistic therapy of Shwachman-Diamond syndrome and prevention of malignant complications due to stem cell manipulation	GGP20008
Pharmacological stimulation of autophagy to rescue proteinopathy and cognitive decline in Mucopolysaccharidosis-IIIA	GSA21D013
Exploit iron-burden astrocytes and mouse models to define the therapy for PKAN and CoPAN	GGP20047
Genome-editing regulation of alternative splicing provides new therapeutic opportunities for episodic ataxia type II	GGP19181
Alternative translation initiation as a novel strategy to block toxicity of the mutant Androgen Receptor in SBMA	GGP19128A
Improving developmental trajectories in 22q11.2 deletion syndrome by oxytocin: focus on anti-inflammatory effects	GGP19103A
GABAA-receptor defects in CDKL5 deficiency disorder: molecular mechanisms and targeting by synthetic neuroactive steroids	GGP20024
Treating cystic fibrosis with a competing peptide targeting PI3Kγ scaffold activity	GGP20079
Allele-specific CRISPR- engineered Cpf1 genome editing to treat ocular surface disorder in ectrodactyly–ectodermal dysplasia–clefting (EEC) syndrome	GGP20088

Pharmacological Degraders for the Cellular Prion Protein	GGP20043
Molecular characterization of early infantile epileptic encephalopathy (EIEE) related HCN1 mutations: advancing therapeutics and treatment	GGP20021
Pharmacological modulation of myelin synthesis and cytoskeletal remodeling as a therapeutic strategy for CMT4B neuropathies with aberrant myelin	GGP20063
SMN circular RNAs as potential new targets and biomarkers for the therapeutic response in Spinal Muscular Atrophy	GGP20055
Pigment Epithelium-derived Factor (PEDF) peptides as therapeutic agents for inherited retinal degeneration	GGP19113
Investigating Ube3a-dependent sumoylation imbalance in the pathogenesis of the Angelman syndrome and autism	GGP20127
Rac GTPase in Intellectual Disability: preclinical opportunities from interfering with a Rac1 protein::protein interaction	GGP20039
MitMed: identification and characterization of new disease genes for mitochondrial disorders	GGP20013
Mitochondrial Ca2+ uptake in the pathogenesis of familial Alzheimer's disease	GGP16029A
Pre-clinical identification of drugs targeting POLG disorders by using a Zebrafish/Yeast trans-species approach (ZIPPY)	GGP19287
Modulation of ADAM10 at the pre- and post-synaptic terminal and its contribution in Huntington's Disease cortico-striatal dysfunction	GGP20067
cGAS-STING driven activation of type-I interferon in Wiskott-Aldrich syndrome	GGP20102
Targeting mitochondria in myopathies with RyR1 and MICU1 mutations	GGP16026
Validation of the human delta globin gene as a therapeutic target for Beta Thalassemia and Sickle Cell Disease	GGP14065
The role of astrocytic mitochondria in 22q11 deletion syndrome	GGP20037
Trial Readiness and Endpoint Assessment in Congenital and Childhood Myotonic Dystrophy	GUP19002H
Dissecting the contribution of altered nuclear mechanotransduction to the pathogenesis of Kabuki Syndrome and its therapeutic implications	GGP20010
Clinical network and Registry for Trial Readiness in Spinal and Bulbar Muscle Atrophy	GUP15009B
Creatine Deficiency Syndrome: novel insight into brain function and therapeutic strategies	GGP19177
UBIAD1 and ferroptosis: exploring a cure for Schnyder Corneal Dystrophy (SCD)	GGP20003
Insight CLN5: Approaching therapies in the neuronal ceroid lipofuscinosis, using Zebrafish as a Tool	GGP20011
PCDH19-related neurodevelopmental syndrome: unraveling the players of neuronal hyperexcitability in search of new therapeutic targets	GGP20056
Developing tools for trial readiness in primary mitochondrial myopathies of the adulthood	GSP16001A
Evidence-based approach to treat hyperexcitability in Rett syndrome through splicing modulation	GGP20016
3D modelling of rare muscular diseases, a powerful platform for basic studies and drug validation	GGP20097

Cone dystrophies and retinal degeneration from protein structures to biological networks. Toward the design of therapeutic molecules	GGP16010B
Cone dystrophies and retinal degeneration from protein structures to biological networks. Toward the design of therapeutic molecules	GGP16010
Targeting mitochondria in myopathies with RyR1 and MICU1 mutations	GGP16026A
Impairment of GABAergic signaling and synaptic plasticity as key determinants for neurodevelopmental disorders: a study from NL3R451C knock-in mice, an animal model of autism	GGP16083

Data di inizio progetto:	**01/01/2021**
Data di fine progetto:	**31/12/2022**

VOCI DI SPESA	COSTO COMPLESSIVO	QUOTA FINANZIATA CON FONDI 5 PER MILLE
Personale di ricerca (borsista, a contratto e di ruolo in quota parte)	645.750,47	594.814,80
Apparecchiature (ammortamento, canone di locazione/leasing)	0	0,00
Materiale d'uso destinato alla ricerca (per laboratori di ricerca, ecc.)	1.732.086,09	1.732.086,09
Spese di organizzazione (manifestazioni e convegni, viaggi, missioni ecc.)	0	
Elaborazione dati	0,00	0,00
Spese amministrative		
Altro (servizi di ricerca)	204.840,69	204.840,69
TOTALE	**2.582.677,25**	**2.531.741,58**

Data, 21/12/22

Il Legale Rappresentante o suo delegato

Si autorizza al trattamento dei dati ai sensi del d.lgs. 196/2003

Il Legale Rappresentante o suo delegato