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 2023
Enti della Ricerca Scientifica

Ente[1]: Fondazione Telethon Ets
Codice fiscale: 04879781005
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Attività:

Il 5 per mille relativo all'anno 2023 è stato recepito dalla Fondazione Telethon Ets nel bilancio al momento dell'emissione delle liste definitive dei beneficiari, avvenuta in data 27/06/2024, quindi attribuito per competenza nel bilancio 2024. L'erogazione dell'importo spettante, pari a € 2570215,32 è avvenuta in data 19/12/2024.

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 (27/06/2024) alla data di incasso più 12 mesi (19/12/2025).

Il criterio di formazione delle poste, conformemente al bilancio di esercizio della Fondazione Telethon Ets, 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 dedicati allo studio e allo sviluppo di terapie innovative per malattie genetiche rare, selezionati tramite i bandi competitivi della Fondazione Telethon ETS e valutati da una commissione internazionale sulla base della qualità scientifica, della solidità metodologica e dell'impatto potenziale sulla vita dei pazienti.

I progetti approvati e oggetto di rendicontazione sono tutti di gestione diretta, e affrontano un ampio spettro di patologie genetiche rare, con approcci multidisciplinari che spaziano dalla ricerca di base alla validazione preclinica di terapie geniche, farmacologiche o basate su tecnologie emergenti.
La ricerca finanziata nel 2023 copre infatti numerosi ambiti: malattie neurologiche, neuromuscolari, metaboliche, malattie del sangue, sindromi dello sviluppo, malattie oculari, patologie mitocondriali e immunologiche. Le attività riguardano modelli cellulari e animali, analisi molecolari, studi funzionali e lo sviluppo di nuove strategie terapeutiche.

Di seguito, a titolo esemplificativo, una descrizione approfondita delle principali aree tematiche e dei progetti rappresentativi.

Malattie neurologiche e disordini del neurosviluppo

Un gruppo significativo di progetti è dedicato allo studio delle malattie neurologiche rare, incluse epilessie genetiche, disordini del neurosviluppo, malattie neurodegenerative ereditarie e sindromi con grave compromissione cognitiva.

Tra queste:

- Sindrome di Rett e disturbi correlati a MECP2 → Progetti come "The interplay between HPCAL4 and MeCP2" (GJC21044/GJC21044A) indagano nuovi regolatori molecolari del segnale neuronale e potenziali bersagli terapeutici.
- Epilessie infantili precoci → Il progetto "Molecular characterization of early infantile epileptic encephalopathy related HCN1 mutations" (GGP20021) studia canali ionici alterati e sviluppa molecole correttive.
- Neurodegenerazione (Huntington) → Progetti come "Deciphering cholesterol efficacy on cognition in prodromal Huntington's disease" (GMR22T1079) analizzano nuovi meccanismi sinaptici e terapie basate su nanoparticelle.
- Autismo e disabilità intellettiva → Diversi progetti esplorano geni chiave come ARHGEF6/Rac1 (GGP20039), PCDH19 (GGP20056), TCF20 (GMR22T1061), con approcci che spaziano dalle cellule staminali ai modelli murini.

Queste ricerche affrontano aspetti cruciali quali la disfunzione sinaptica, l'alterata comunicazione neurone–astroglia, la compromissione dell'eccitabilità neuronale, e la possibilità di intervenire su pathway molecolari specifici con farmaci innovativi o terapie geniche.

Malattie metaboliche e mitocondriali

Numerosi progetti indagano patologie causate da difetti bioenergetici, alterata funzione mitocondriale o compromissione delle vie metaboliche cellulari.

Esempi rappresentativi:

- Disordini mitocondriali pediatrici → Il progetto MitMed (GGP20013) amplia il catalogo dei geni causa di malattie mitocondriali e sviluppa modelli animali e cellulari dedicati ().
- MERRF e altre encefalopatie mitocondriali → "Cure MERRF: from fibroblasts to organoids" (GGP20115) utilizza organoidi derivati da iPSC per testare terapie di nuova generazione.
- SPG7 e paraplegia spastica ereditaria → Il progetto GMR22T2019 studia il regolatore del mitocondrio mPTP allo scopo di individuare farmaci riposizionabili efficaci
- PKAN e CoPAN → GGP20047 studia la neurodegenerazione da accumulo di ferro e indaga trattamenti basati su CoA, deferiprone e molecole candidate.

In tutti questi casi i ricercatori puntano a chiarire come disfunzioni mitocondriali causino danno cellulare, neurodegenerazione o alterazioni neurometaboliche, sviluppando modelli preclinici e terapie mirate.

Malattie del sangue e del sistema immunitario

Le patologie ematologiche rare rappresentano un ulteriore filone importante.

Tra i progetti inclusi:

- Emofilia e disturbi della coagulazione → In GMR22T1059 si studiano le cause vascolari del sanguinamento in trombastenia di Glanzmann, con analisi su cellule endoteliali derivate dai pazienti.
- Beta-emoglobinopatie → Progetti come GGP20046 testano strategie per aumentare l'emoglobina A2 come terapia per la β-talassemia.

Sickle Cell Disease → GGP20116 analizza i pathway pro-resolving dell'infiammazione per ridurre le complicanze cardiovascolari.

Malformazioni congenite e difetti dello sviluppo

Alcuni progetti esplorano patologie genetiche che alterano lo sviluppo embrionale, scheletrico, craniofacciale e neurocognitivo.

Esempi chiave:

- Sindrome 22q11.2 → Il progetto GGP19103 studia gli effetti dell'ossitocina su fenotipi immunitari, cognitivi e sociali.
- Cole Carpenter Syndrome → GGP20074 analizza le conseguenze della mutazione PDI sulla fragilità ossea.
- Catel-Manzke syndrome → GMR22T1065 approfondisce il ruolo del gene TGDS nella condrogenesi e sintesi dei glicosaminoglicani.
- Neurocristopatie da mutazioni NKTR → GMR22T1054 studia lo splicing e la migrazione delle cellule della cresta neurale.

Malattie oftalmiche e degenerazioni retiniche

Diversi progetti sono dedicati alle distrofie retiniche ereditarie e alle neuropatie visive.

Tra questi:

- Retinite pigmentosa e neuroprotezione retinica → GGP19113 sviluppa peptidi PEDF e terapie geniche per proteggere i fotorecettori.
- EEC syndrome e difetti corneali → GGP20088 studia l'editing allelico specifico con CRISPR-Cpf1.

Retina artificiale non genetica → GMR22T2013 testa composti foto-switch per ripristinare la visione in modelli di Retinite pigmentosa.

Malattie neuromuscolari

- Tra i progetti dedicati alle patologie dei muscoli e dei nervi periferici:
- Charcot-Marie-Tooth (CMT) neuropathies → Diversi progetti (GGP20063, GMR22T1003, GGP20003) investigano mTORC1, il rimodellamento della mielina, la ferroptosi e nuove terapie.
- Distrofie muscolari, inclusa Duchenne → GMR22T1020 e GMR22T2016 esplorano nuovi target quali SIRT6 e le modulazioni della permeabilità mitocondriale.
- Miopatie da alterazioni del calcio (Tubular Aggregate Myopathy) → GMR22T1090 studia canali STIM/ORAI e possibili farmaci inibitori.

Conclusione

- Nel complesso, i progetti finanziati con il cinque per mille 2023 rappresentano un programma scientifico ampio, multidisciplinare e altamente innovativo, volto a generare conoscenze fondamentali e potenziali soluzioni terapeutiche per numerose malattie genetiche rare, spesso prive di cura.

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

Commessa	Title
GGP19002	Knockdown and Replacement of MFN2: a Gene Therapy to treat Dominantly Inherited Peripheral Neuropathy CMT2A
GGP19103	Improving developmental trajectories in 22q11.2 deletion syndrome by oxytocin: focus on anti-inflammatory effects
GGP19113	Pigment Epithelium-derived Factor (PEDF) peptides as therapeutic agents for inherited retinal degeneration
GGP20003	UBIAD1 and ferroptosis: exploring a cure for Schnyder Corneal Dystrophy (SCD)
GGP20008	Ribosomal pathologies: mechanistic therapy of Shwachman-Diamond syndrome and prevention of malignant complications due to stem cell manipulation
GGP20010	Dissecting the contribution of altered nuclear mechanotransduction to the pathogenesis of Kabuki Syndrome and its therapeutic implications
GGP20011	Insight CLN5: Approaching therapies in the neuronal ceroid lipofuscinosis, using Zebrafish as a Tool
GGP20013	MitMed: identification and characterization of new disease genes for mitochondrial disorders
GGP20016	Evidence-based approach to treat hyperexcitability in Rett syndrome through splicing modulation
GGP20021	Molecular characterization of early infantile epileptic encephalopathy (EIEE) related HCN1 mutations: advancing therapeutics and treatment
GGP20024	GABAA-receptor defects in CDKL5 deficiency disorder: molecular mechanisms and targeting by synthetic neuroactive steroids
GGP20037	The role of astrocytic mitochondria in 22q11 deletion syndrome
GGP20039	Rac GTPase in Intellectual Disability: preclinical opportunities from interfering with a Rac1 protein::protein interaction
GGP20043	Pharmacological Degraders for the Cellular Prion Protein
GGP20046	THE HUMAN δ-GLOBIN GENE AS A THERAPEUTIC TOOL FOR β-HEMOGLOBINOPATHIES. POST GWAS TARGET VALIDATION AND EVALUATION OF MOLECULES IN PRECLINICAL MODELS.
GGP20047	Exploit iron-burden astrocytes and mouse models to define the therapy for PKAN and CoPAN.
GGP20055	SMN circular RNAs as potential new targets and biomarkers for the therapeutic response in Spinal Muscular Atrophy
GGP20056	PCDH19-related neurodevelopmental syndrome: unraveling the players of neuronal hyperexcitability in search of new therapeutic targets
GGP20063	Pharmacological modulation of myelin synthesis and cytoskeletal remodeling as a therapeutic strategy for CMT4B neuropathies with aberrant myelin.
GGP20065	Detailing and modeling dendritic spine pruning pathways and cognition in Rab39b XLID mouse model
GGP20070	Joubert syndrome: beyond conventional mendelian genetics
GGP20073	Cell-based therapy for Congenital Thrombotic Thrombocytopenic Purpura
GGP20074	In-depth phenotyping and experimental therapy of Cole Carpenter Syndrome
GGP20079	Treating cystic fibrosis with a competing peptide targeting PI3Kγ scaffold activity
GGP20088	Allele-specific CRISPR- engineered Cpf1 genome editing to treat ocular surface disorder in ectrodactyly–ectodermal dysplasia–clefting (EEC) syndrome
GGP20101	Metabolism of polysialic acid: new insight into pathological mechanisms and potential treatments for Huntington's disease
GGP20102	cGAS-STING driven activation of type-I interferon in Wiskott-Aldrich syndrome
GGP20105	Patient-specific molecular mechanisms of Fragile X Syndrome pathogenesis and Fragile-X associated phenotypes
GGP20115	Cure MERRF: from fibroblasts to organoids speeding basic science into clinical trials for mitochondrial diseases
GGP20116	IDENTIFICATION OF DRUGGABLE PRO-RESOLVING MECHANISMS IN SICKLE CELL DISEASE
GGP20124	Novel therapeutic approaches for AEC syndrome
GGP20127	Investigating Ube3a-dependent sumoylation imbalance in the pathogenesis of the Angelman syndrome and autism
GGP20128	Liver-directed promoterless gene targeting without the use of nucleases as a potential therapy for Fabry disease
GGP20130	Illuminating the biology of the GPR101 receptor: analysis of its transcriptional regulation and validation of new ligands
GGP20137	A new RNA-based therapy for the Fragile X Syndrome
GJC21014	Pathological molecular mechanisms underlying APOPT1 loss of function
GJC21015	Functional characterization of the InSyn1-CDKL5 interaction for dystrophin/dystroglycan complex dependent inhibitory synapse formation
GJC21035	Assessing the consequences of AMPARs defective transport in an AP4 deficiency mouse model
GJC21044	The interplay between HPCAL4 and MeCP2: identification and characterization of a novel putative target for Rett syndrome therapy
GJC21044A	The interplay between HPCAL4 and MeCP2: identification and characterization of a novel putative target for Rett syndrome therapy
GJC21065	Dissecting the pathomolecular mechanisms of Prr12 gene inactivation leading to neurodevelopmental and eye abnormalities.
GJC21065A	Dissecting the pathomolecular mechanisms of Prr12 gene inactivation leading to neurodevelopmental and eye abnormalities.
GJC21084	At the origin of congenital muscular dystrophy: shedding light on the Tdark proteins DPM2 and DPM3
GJC21084A	At the origin of congenital muscular dystrophy: shedding light on the Tdark proteins DPM2 and DPM3
GJC21115	Defining VPS13D's function(s) to reveal the pathogenetic mechanism causing VPS13D-linked movement disorders
GJC21131	Delving into the mechanisms underlying HPDL-related disorders with a multi-model approach
GJC21131A	Delving into the mechanisms underlying HPDL-related disorders with a multi-model approach
GJC21144	Dissecting MLIP role in the molecular cascade triggered by lamina dysfunction in Emery Dreifuss Muscular Dystrophy
GJC21144A	Dissecting MLIP role in the molecular cascade triggered by lamina dysfunction in Emery Dreifuss Muscular Dystrophy
GJC21157	Discovery of novel genes involved in Huntington's Disease pathogenesis
GJC21157A	Discovery of novel genes involved in Huntington's Disease pathogenesis
GMR22T1003	Boosting HSPB3 to prevent neuromuscular degeneration in peripheral neuropathies
GMR22T1012	Mechanisms of cardiopharyngeal differentiation
GMR22T1020	Harnessing the Sirtuin 6-Thyroid Hormone cross talk to counteract the progression of the Duchenne Muscular Dystrophy
GMR22T1027	Understanding the role of CNBP-eIF5A-polyamine metabolism in DM2 pathogenesis
GMR22T1029	Mechanisms and disease models of neurodevelopmental disorders involving CLC anion transporters
GMR22T1031	Role of astrocyte Ca2+ signaling for hippocampal spatial memory in a mouse model of familial Alzheimer's Disease
GMR22T1035	Identification of New Biomarkers Monitoring DMD Pathology and Response to Treatment
GMR22T1039	The role of ancient gene variants in Prader-Willi syndrome pathophysiology
GMR22T1041	The natural antisense lncRNA PHOX2B-AS1 in the pathogenesis and as potential drug target in Congenital Central Hypoventilation Syndrome (CCHS)
GMR22T1053	Role of myeloperoxidase-mediated neuroinflammation in aceruloplasminemia
GMR22T1054	Connecting craniofacial malformations with neural crest splicing defects by defining the role of nuclear cyclophilin NKTR
GMR22T1055	Defining the role of skeletal muscle peroxisomes in Zellweger Spectrum Disorders
GMR22T1059	Contribution of vascular abnormalities to gastrointestinal bleeding in patients with Glanzmann Thrombasthenia: mechanistic studies using endothelial colony forming cells (ECFCs)

GMR22T1061	Identification of possible therapeutic targets to rescue neuronal and synaptic dysfunctions caused by deletions and mutations of the TCF20 intellectual disability gene
GMR22T1065	Role of TGDS in Catel-Manzke syndrome
GMR22T1066	Targeting oligodendroglial cell dysfunctions to treat cognitive defects and epilepsy in primary autosomal recessive microcephaly-17 (MCPH17) models
GMR22T1067	Study of the amyloidogenic conversion of V30M, S52P and V122I transthyretin variants by real-time Nuclear Magnetic Resonance: elucidation of the molecular mechanisms leading to different ATTR amyloidosis severity and different drug response.
GMR22T1071	Modeling Pitt-Hopkins syndrome and new pathogenetic variants of TCF4 by gene editing: a step forward toward personalized medicine (HOPeFOR)
GMR22T1076	Posterior Column Ataxia and Retinitis Pigmentosa: new pathogenetic insights from the study of mitochondria-associated membranes
GMR22T1078	An in vivo model of intractable R257C-ACTG2 Visceral Myopathy to study pathogenesis and to identify new disease targets
GMR22T1079	Deciphering Cholesterol efficacy on cognition in prodromal Huntington's disease
GMR22T1081	Toler8: Uncovering the dynamics of cellular and molecular pathways for immune tolerance in hemophilia A
GMR22T1082	Proteinopathy and lysosomal dysfunction in Sanfilippo disease: linking mechanisms and role in neuroinflammatory astrocytes
GMR22T1086	Impact of a novel variant of the beta isoform of the TBXA2R gene associated with a hemorrhagic disorder on platelet and endothelial function
GMR22T1088	Molecular mechanisms underlying Joubert syndrome
GMR22T1090	Understanding the basis of tubular aggregate myopathy
GMR22T1093	At The HEart of laminopathies: development of subtype-specific cardiomyocyte models to unravel distinct cellular mechanisms of LMNA-cardiomyopathy (ATHENA)
GMR22T1100	Disease-Modifying Therapeutic Approaches in a Gene-Edited Model of Timothy Syndrome
GMR22T2013	Development and application of novel membrane-targeted photoswitches for restoration of the physiological retinal processing in Retinitis pigmentosa (LIGHTSWITCH)
GMR22T2016	A mitochondrial therapy for muscular dystrophies
GMR22T2018	Correcting FOXG1 activity levels by small RNA-analogs modulating the corresponding mRNA levels and their translation rates
GMR22T2019	Regulating the mitochondrial permeability transition pore for treating hereditary spastic paraplegia type 7 (SPG7)
GMR22T2020	Pharmacologic activation of the ATF6 branch of the UPR for therapeutic intervention in CMT1B neuropathy
GMR23T1018	Characterization of a new therapeutic strategy for Phelan McDermid syndrome by rescuing dysregulated protein synthesis
GMR23T1020	Exploring the role of Interleukin-6 (IL-6) in Rett syndrome: focus on astrocyte-neuron communication
GMR23T1022	Dissecting the role of Sox2 in neurons of the visual thalamus: insights into developmental visual disorders
GMR23T1032	Targeting overexpressed transcription co-regulators to suppress SBMA

GMR23T1033	DONOR: MoDeling ChrOnic INtestinal Pseudo-Obstruction with RAD21-dependent Molecular Mechanisms
GMR23T1035	Understanding the causes and consequences of inflammation in FSHD muscular dystrophy to develop a possible treatment
GMR23T1036	Targeting Interleukin 17F during nontuberculous mycobacterial lung infection in cystic fibrosis
GMR23T1037	Unraveling the role of ineffective erythropoiesis in diabetes development in β-thalassemia
GMR23T1048	Ribosome associated proteins as the next-generation therapy for Spinal Muscular Atrophy
GMR23T1055	Role of Cl- homeostasis in aberrant brain rhythms, from oscillations to sleep-wake cycles, in a mouse model of intellectual disability and autism spectrum disorder.
GMR23T1059	Unravelling the role of DNA on its own instability within the Huntington's disease locus
GMR23T1060	Dissecting the role of cytoplasmic signaling metabolites in Niemann-Pick disease type C
GMR23T1062	Deciphering the role of the maternal-effect gene PADI6 in the etiology of genomic imprinting defects
GMR23T1065	Unravelling the function of MPV17
GMR23T1066	Modelling ADA-SCID neuropathology at scale using patient-derived organoids
GMR23T1193	Role of Aquaporin-4 isoform mutations in megalencephalic leukoencephalopathy with subcortical cysts
GMR23T1197	Role of Negr1 signaling dysregulation in Fragile X and other rare syndromic forms of autism.
GMR23T1234	Astrocyte Calcium Rescue to Overcome Familial Alzheimer's vascular Dysfunction (ACROFAD)
GMR23T2003	Delivery of cytoplasmic HDAC4 to treat DMD
GMR23T2007	Selective control of DNA damage response at telomeres as an innovative therapeutic approach for Dyskeratosis Congenita
GMR23T2008	Exploring a new therapeutic target for Niemann-Pick C1 disease: the BET proteins
GMR23T2011	Nav1.1 translation enhancement-based therapy to treat Dravet Syndrome
GMR23T2012	A multitask lentiviral vector for ex vivo gene therapy of Duchenne Muscular Dystrophy
GMR23T2014	Treating autosomal dominant polycystic kidney disease by using inhalable thyroid hormone-nanocarriers
GMR23T2021	A redox cycler-based therapeutic strategy against respiratory chain dysfunction-related mitochondrial diseases: towards the clinic
GMR23T2024	GBA1-derived Nanobodies as a novel therapeutic strategy in neuropathic Gaucher disease
GMR23T2152	DeveLopment of a pharmacologIcal neonatal treatment and an in uterO fetal gene therapy for leigh syNdrome - LION
GMR23T2157	Development and application of spastin recovery therapeutic approaches in SPG4-HSP pre-clinical models
GMR23T2182	Sphingolipid metabolic imbalance in murine and hiPSC RTT models: development of a drug repurposing-based therapy

Data di inizio progetto:	**27/06/2024**
Data di fine progetto:	**19/12/2025**

VOCI DI SPESA	COSTO COMPLESSIVO	QUOTA FINANZIATA CON FONDI 5 PER MILLE
Personale di ricerca (borsista, a contratto e di ruolo in quota parte)	452.577,60	225.458,96
Apparecchiature (ammortamento, canone di locazione/leasing)		
Materiale d'uso destinato alla ricerca (per laboratori di ricerca, ecc.)	1.994.268,89	1.994.268,89
Spese di organizzazione (manifestazioni e convegni, viaggi, missioni ecc.)		
Elaborazione dati		
Spese amministrative		
Altro (servizi di ricerca)	350.487,47	350.487,47
TOTALE	**2.797.333,96**	**2570215,3**

Roma,

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Data: 18/03/2026 16:03:41

Direttore Generale di Fondazione Telethon
Ilaria Villa

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

Direttore Generale di Fondazione Telethon
Ilaria Villa

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Data: 18/03/2026 16:03:40