# Biobanks and registries - what's the difference?

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FONDAZIONE Telethon

# Overview

1. What is a biobank
2. What is a registry

- What sort of research do they support
- How they operate
- Examples

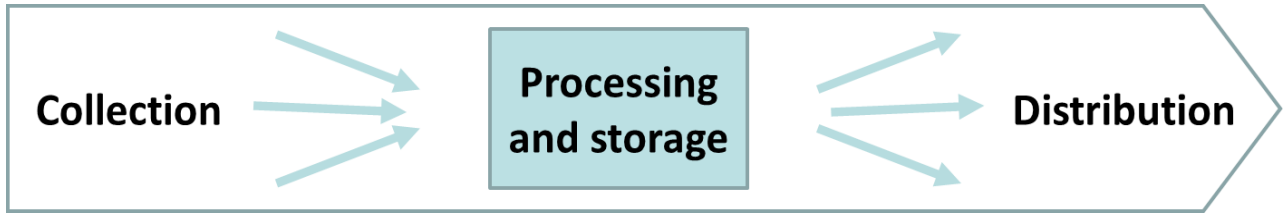
3. Biobank VS Registry

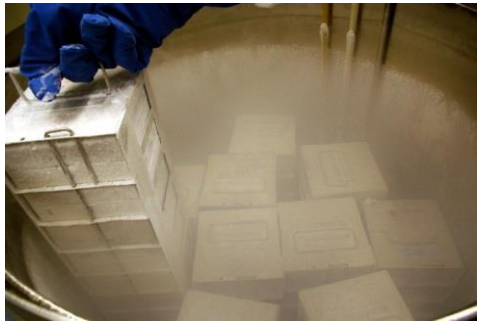
- Similarities
- Differences
- Synergies

# What is a biobank?

**Biobank** is an organised collection of human biological material and associated information stored **for one or more research purposes**

Kauffmann & Cambon-Thomsen, 2008 *JAMA*



# Types of research biobanks

| | |
|---|---|
| **Disease based** | Contain biological samples taken from patients with specific diseases, from carriers and health control individuals. eg. Cancer, cystic fibrosis, etc. |
| **Cohort Based (longitudinal /isolated)** | Contain samples from subsets of a population with or without a certain diseas, eg. regions, ethnicities. Contain homogenous genetic material of the population. |

# Biobanks may differ from each other

**Size**

hundreds – millions of biological samples

**Geographical coverage**

regional, national, international

**Hosting organisation**

university, hospital, companies, foundations, etc

**Types of sample stored**

blood, urine, cells, DNA, tissues, etc

**Additinal services**

performing experiments, quality validation, additional sample derivatives, services on request

# NOT considered as research biobanks

**Project-based sample collections**

**Repositories of biological material having specific regulations**

- Organs for transplant
- Samples for therapeutic purposes, skin burns
- Blood for transfusion
- Embryos, sperm, oocytes for IVF

**(Repositories of human tissue created for diagnostic or clinical purposes)**

Guthrie cards/dried blood cards

**Collections of samples and data made for obtaining regulatory approval**

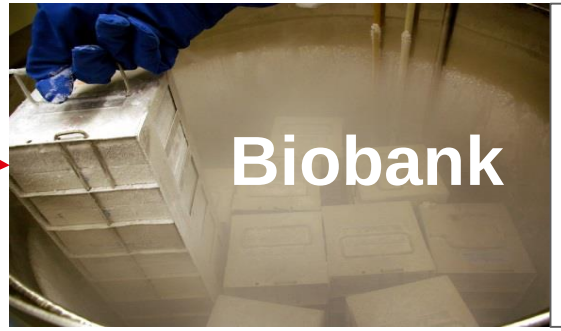
eg. Clinical trials for new drugs

# Central biobank workflow

**Patients, Participants**

***Informed Consent***

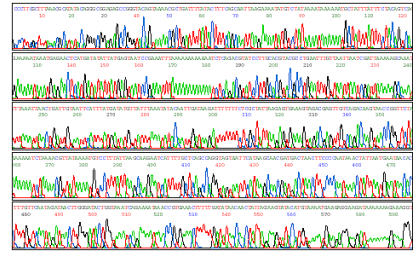

Blood, cells, DNA, urine, etc




**Request access**

**Users**

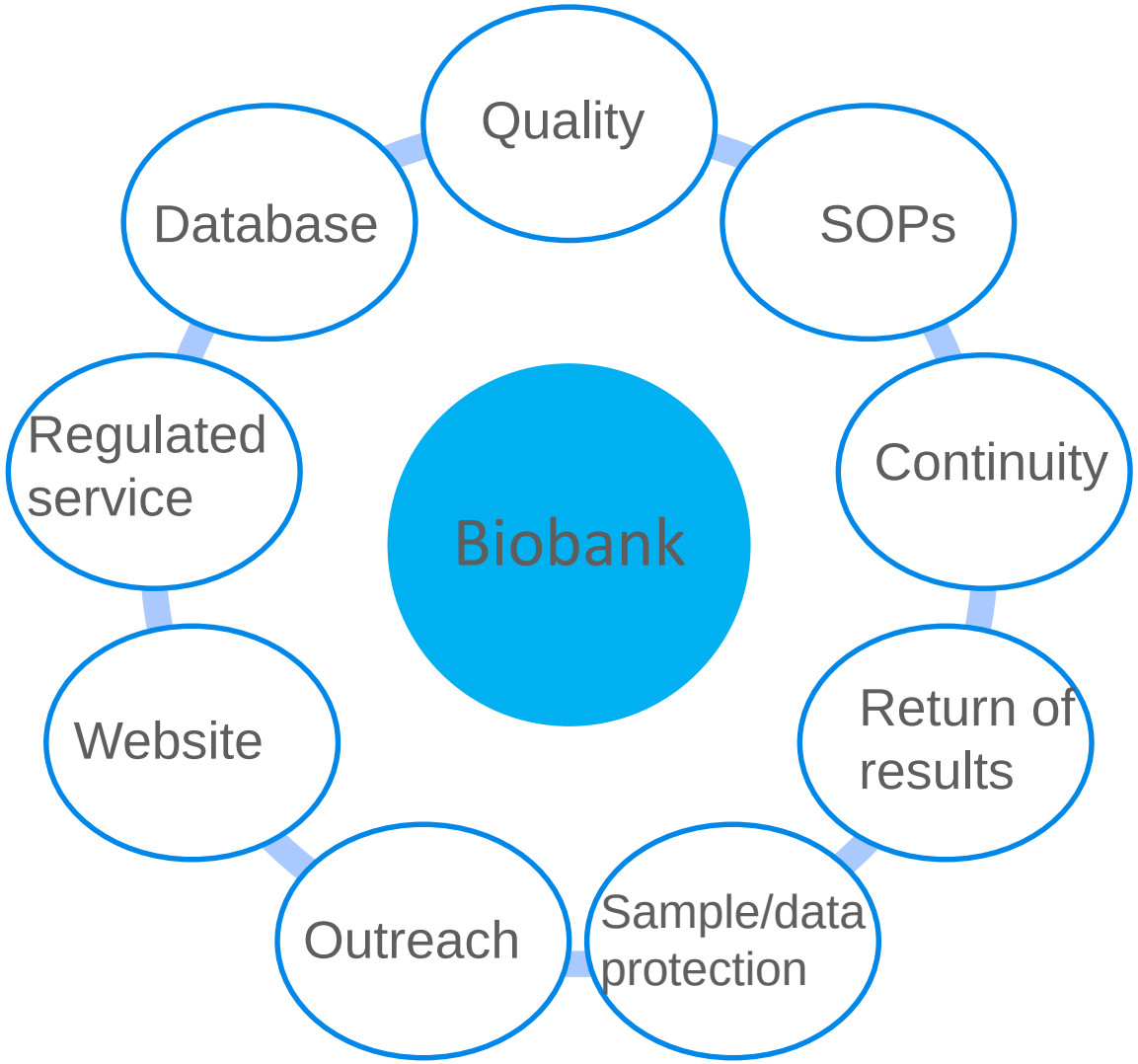
***Material Transfer Agreement***

# How does a biobank operate?

**Professional research infrastructure to:**

- broker access for researchers who might not otherwise be able to access the needed materials for their research.
- warrant the quality of the biological materials over time; support research reproducibility and openness to future research technologies.
- manage the related ethical and legal issues.



# Biobanks support future research advancement

## 1999

5 male babies died in early infancy in Italian family due to a rare immunodeficiency disorder **IPEX**
*(immunodysregulation polyendocrinopathy enteropathy X-linked)*

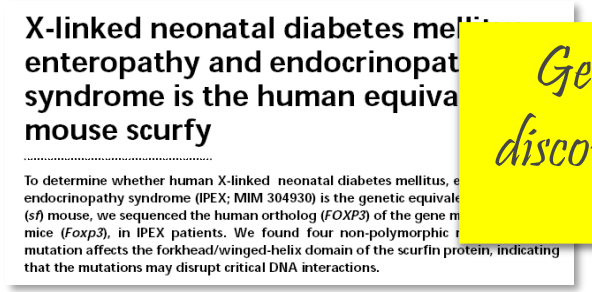
Genetic counselling
**Deposit of biological samples in a Biobank**

*Samples banked*

## 2001

Scientists in USA requested these samples and identified FOXP3 as causative gene for IPEX.

*Wildin et al., 2001 Nat Genet*

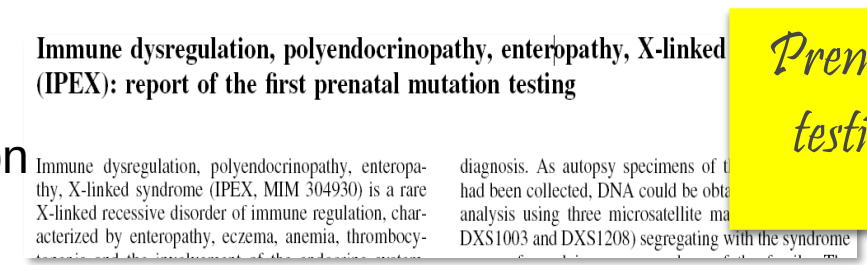

X-linked neonatal diabetes mel
enteropathy and endocrinopat
syndrome is the human equiva
mouse scurfy

To determine whether human X-linked neonatal diabetes mellitus, e
endocrinopathy syndrome (IPEX; MIM 304930) is the genetic equivale
(*sf*) mouse, we sequenced the human ortholog (*FOXP3*) of the gene m
mice (*Foxp3*), in IPEX patients. We found four non-polymorphic
mutation affects the forkhead/winged-helix domain of the scurfin protein, indicating
that the mutations may disrupt critical DNA interactions.

*Gene discovery*

## 2006

Samples used in the development and validation of the first genetic test for prenatal diagnosis


Immune dysregulation, polyendocrinopathy, enteropathy, X-linked
(IPEX): report of the first prenatal mutation testing

Immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX, MIM 304930) is a rare X-linked recessive disorder of immune regulation, characterized by enteropathy, eczema, anemia, thrombocy-

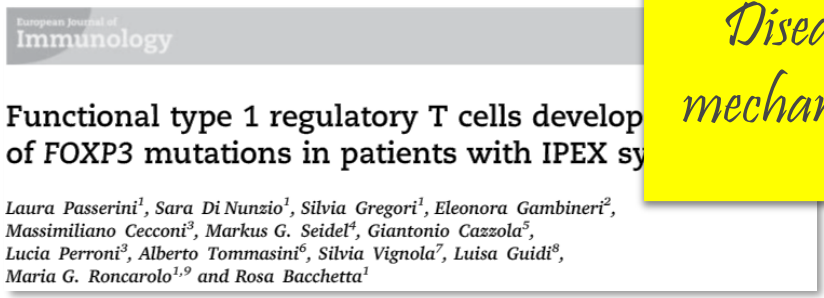
diagnosis. As autopsy specimens of t
had been collected, DNA could be obta
analysis using three microsatellite ma
DXS1003 and DXS1208) segregating with the syndrome

*Perroni et al., 2006 Prenat Diagn*

*Prenatal testing*

## 2011

Samples used in pathophysiology studies


European Journal of Immunology

Functional type 1 regulatory T cells develop
of FOXP3 mutations in patients with IPEX sy

*Laura Passerini[1], Sara Di Nunzio[1], Silvia Gregori[1], Eleonora Gambineri[2], Massimiliano Cecconi[3], Markus G. Seidel[4], Giantonio Cazzola[5], Lucia Perroni[3], Alberto Tommasini[6], Silvia Vignola[7], Luisa Guidi[8], Maria G. Roncarolo[1,9] and Rosa Bacchetta[1]*

*Passerini et al., 2011 Eur J Immunol*

*Disease mechanism*

NETWORK OF GENETIC BIOBANKS
Telethon



*Biobank: now at Gaslini Children's Hospital, Genoa, Italy*

# Providing answers and hope to families

http://www.bbmri-eric.eu/blog/reaching-diagnosis-storing-biosamples-biobank/

## Nicla and Raffaella

No diagnosis for over 20 years.

DNA deposited in biobanks led to discovery of a new genetic disease IDDCA (Intellectual developmental disorder with cardiac arrhythmia)

REPORT

2016

*GNB5* Mutations Cause an Autosomal-Recessive Multisystem Syndrome with Sinus Bradycardia and Cognitive Disability

Elisabeth M. Lodder,[1,22] Pasquelena De Nittis,[2,3,22] Charlotte D. Koopman,[4,5,22] Wojciech Wiszniewski,[6] Carolina Fischinger Moura de Souza,[7] Najim Lahrouchi,[1] Nicolas Guex,[2,8] Valerio Napolioni,[9] Federico Tessadori,[5] Leander Beekman,[1] Eline A. Nannenberg,[10] Lamiae Boualla,[11] Nico A. Blom,[12] Wim de Graaff,[13] Maarten Kamermans,[13,14] Dario Cocciadiferro,[3,15] Natascia Malerba,[3,15] Barbara Mandriani,[3,16] Zeynep Hande Coban Akdemir,[6] Richard J. Fish,[17] Mohammad K. Eldomery,[6] Ilham Ratbi,[11] Arthur A.M. Wilde,[1] Teun de Boer,[4] William F. Simonds,[18] Marguerite Neerman-Arbez,[17] V. Reid Sutton,[6,19] Fernando Kok,[20] James R. Lupski,[6,19,21] Alexandre Reymond,[2,23] Connie R. Bezzina,[1,23] Jeroen Bakkers,[4,5,23,*] and Giuseppe Merla[3,23,*]

Stem Cell Research 40 (2019) 101547

Contents lists available at ScienceDirect

Stem Cell Research

journal homepage: www.elsevier.com/locate/scr

Lab Resource: Multiple Cell Lines

Generation of the induced human pluripotent stem cell lines CSSi009-A from a patient with a *GNB5* pathogenic variant, and CSSi010-A from a CRISPR/Cas9 engineered *GNB5* knock-out human cell line

Natascia Malerba[a], Patrizia Benzoni[b], Gabriella Maria Squeo[a], Raffaella Milanesi[b], Federica Giannetti[b], Lynette G. Sadleir[c], Gemma Poke[c], Bartolomeo Augello[a], Anna Irma Croce[a], Andrea Barbuti[b], Giuseppe Merla[a,*]

2019

*Biobank: Casa Sollievo della Sofferenza Hospital in S. Giovanni Rotondo, Italy*

# What is a registry?

An organised system that uses observational methods to collect uniform data on a patient population defined by a particular disease, exposure or condition (e.g. age, pregnancy, specific patient characteristics), and which is followed over time.

Patient disease registries may be established by public organisations such as *academia* or medical *research associations* of *health care* professionals or *patients*.

They may have different objectives, such as:

- To describe the natural history of a disorder,
- to monitor the efficacy or safety of treatments,
- to describe the impact of a disease on patients' health and quality of life or
- to identify patients suitable for new treatments.

*European Medicine Agency, EMA/763513/2018*

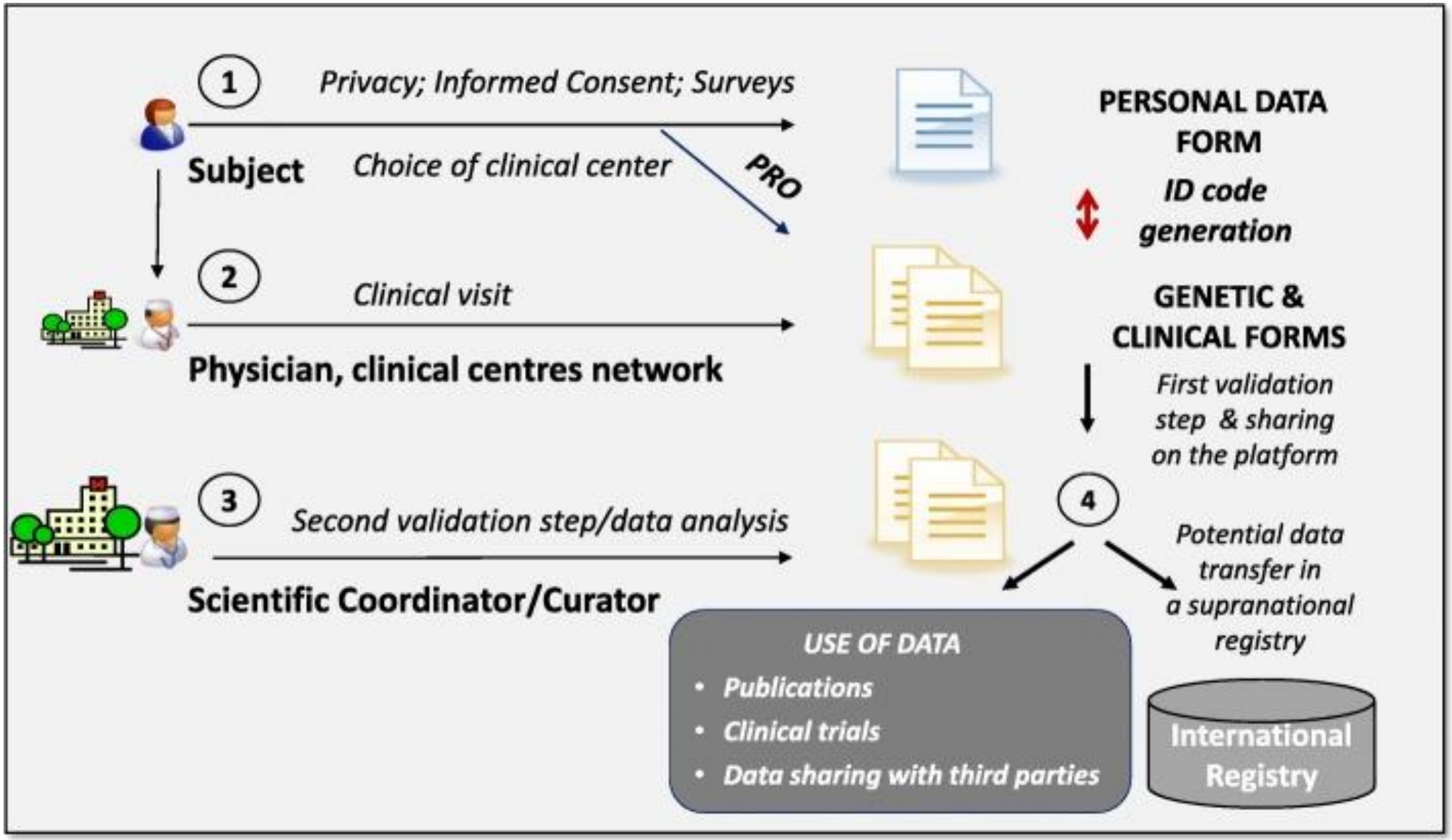
# Data collection in registries

- Subject info: Patient ID, consent, demongraphic, date of birth, place of birth, address, social security, etc
- Medical history
- Environmental exposure
- Patient characteristics: Quality of life, occupation, diet, lifestyles.

| | | |
|---|---|---|
| **2.** | **Genetic test result**<br><br>o Confirmed FSHD1 (with details)<br>o Confirmed FSHD2 (with details)<br>o Result pending<br>o Not tested | **What is your genetic test result?**<br><br>o I have been told I have genetically confirmed FSHD and I can provide a copy of my genetic test result<br>o I have been told I have genetically confirmed FSHD and I give the registry permission to ask my doctor for my genetic test result<br>o I have been tested but I haven't received the result yet<br>o I have not been tested |
| **3.** | **Clinical Diagnosis**<br><br>o no signs or symptoms<br>o Facial weakness<br>o Periscapular shoulder weakness<br>o Foot dorsiflexor weakness<br>o Hip girdle weakness | **Which of these symptoms do you have? (Tick all that apply)**<br><br>o I have no signs or symptoms of muscle weakness<br>o Facial weakness<br>(weakness of muscles in the face causing e.g. inability to smile, to whistle, or to close your eyes fully at night)<br>o Shoulder weakness<br>(weakness of the muscles around the shoulder blades causing e.g. inability to raise your arms sideways above the level of your shoulder)<br>o Foot weakness<br>(weakness of the muscles that help you lift your feet up, |

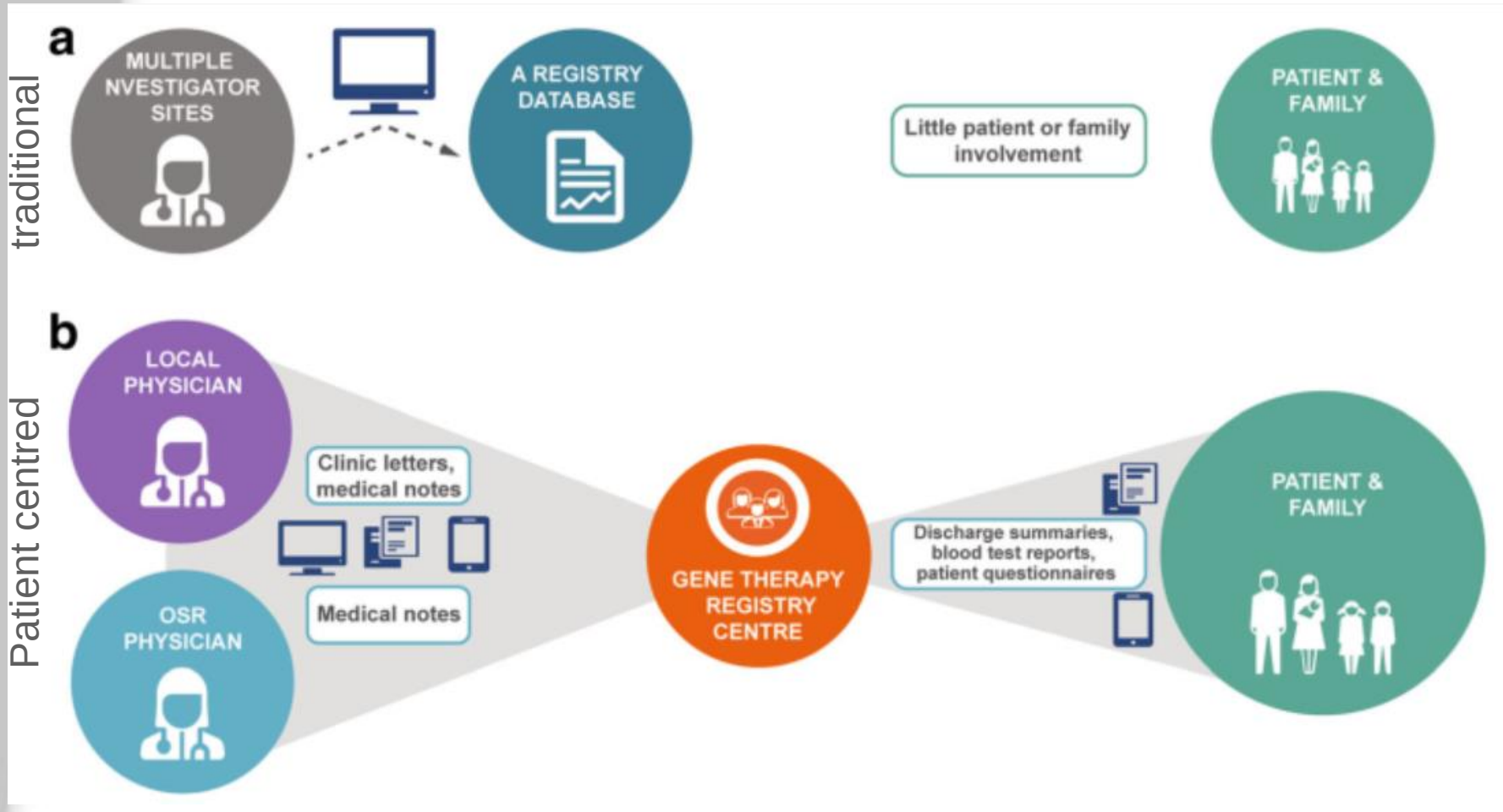
*UK FSHD Patient Registry Core Data Element 2011*

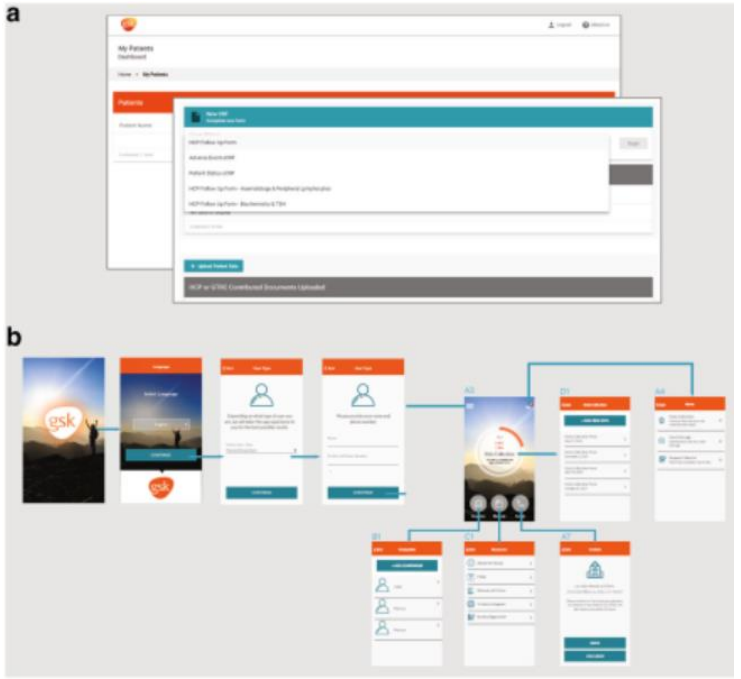
# Registry workflow




Ambrosini A et al., 2018 Orphanet J Rare Dis

# Patient-centric registry




Stirnadel-Farrant H et al., 2018 Orphanet J Rare Dis

# Elements to consider when setting up a registry

- **Patient population**: enrolment of patients and avoid selection bias.
- **Time elements**: accurate knowledge and recording of dates of important events.
- **Core data elements**: a list of core data elements to be collected in all patients is proposed.
- **Terminologies**: common terminologies for diseases, diagnostic tests, symptoms and other relevant data. Local or national terminologies should be mapped to international terminologies.
- **Quality management:** ensure data accuracy and timeliness.
- **Safety analysis:** registries conducted by organisations such as academia or medical research associations should follow the national requirements.
- **Governance:** Most registries have a governance model relying on principles and constraints based on their mandate, operating procedures, legal environment or funding sources. Principles of data ownership, informed consent and data security in accordance with the General Data Protection Regulation (GDPR).

*European Medicine Agency, EMA/763513/2018*

# Registry in steps of drug development

design of clinical trials, inclusion criteria

Clinicians

Support regulatory, reimbursement decisions

Regulatory Authority

Discovery | Pre-Clinical | Clinical | Market Authorisation | Post-Authorisation

Natural history studies, quality of life measures

Researchers

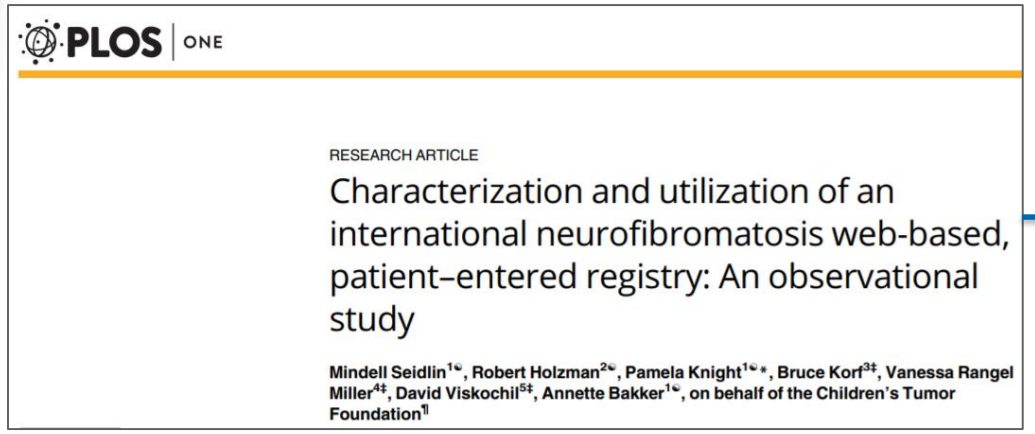
Identify suitable patients for trials

Industry

Safety, effectiveness evidence, real world monitoring

Patients
Patient organisations

# Examples of registries in use



PLOS ONE

RESEARCH ARTICLE

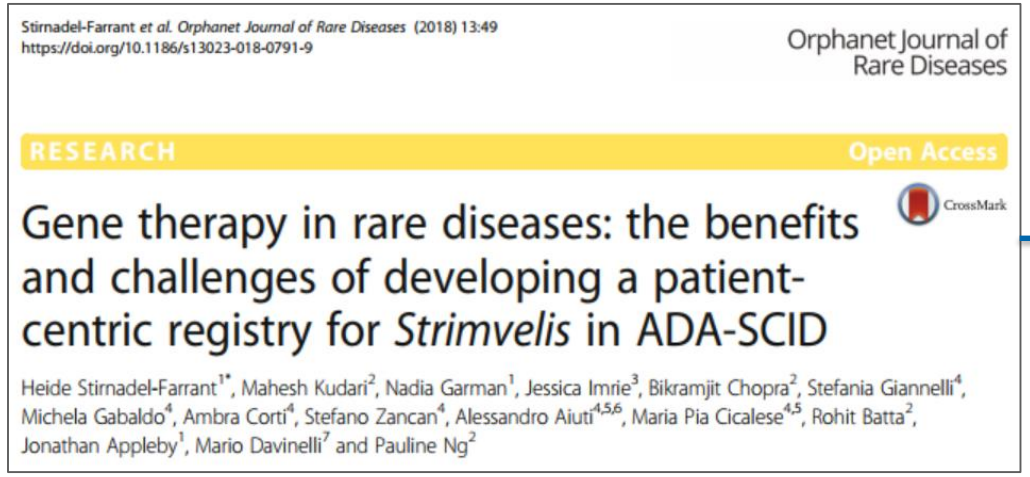
Characterization and utilization of an international neurofibromatosis web-based, patient–entered registry: An observational study

Mindell Seidlin[1☯], Robert Holzman[2☯], Pamela Knight[1☯*], Bruce Korf[3‡], Vanessa Rangel Miller[4‡], David Viskochil[5‡], Annette Bakker[1☯], on behalf of the Children's Tumor Foundation[¶]

| | Start Date | Population | Type of study | Email sent |
|---|---|---|---|---|
| 1 | Apr 2013 | NF1, Tibial bowing | Observational | 256 |
| 2 | Mar 2014 | NF1, NF2—Adult | Intervention: Behavioral | 1465 |
| 3 | May 2014 | NF1, NF2—Adolescent | Observational: Focus Group | 813 |
| 4 | Sep 2015 | NF1, NF2—Adolescent | Intervention: Behavioral | 1840 |
| 5 | Jul 2015 | NF1, ages 16–34, plexiform neurofibroma | Intervention: Behavioral | 1019 |
| 6 | May 2015 | NF1, ages 3–31, MPNST | Intervention: Drug -Phase II | 668 |
| 7 | Mar 2015 | NF2, ages 12–40,vestibular schwannoma | Intervention: Drug –Phase II | 141 |
| 8 | Dec 2014 | NF1, ages2-18,plexiform neurofibroma | Observational- Focus group | 366 |
| 9 | Apr 2015 | NF1 ages 8–12, plexiform neurofibroma | Observational- Focus group | 154 |
| 10 | Jun 2015 | NF1 ages 5–7,plexiform neurofibroma | Observational- Focus group | 640 |
| 11 | May 2013 | NF1 ages 7–16 | Observational | 500 |
| 12 | Mar 2014 | NF1, MPNST* | Intervention: Radiation | 39 |
| 13 | Jul 2013 | NF1, breast cancer | Observational | 3 |
| 14 | Feb 2015 | NF1, parents of affectedchildren | Observational | 1605 |
| 15 | Mar 2016 | NF1, Adult, UK,plexiform neurofibroma | Observational: QoLquestionnaire development | 37 |
| 16 | Mar 2015 | NF1, pain | Observational: Questionnairedevelopment | 3187 |
| 17 | Oct 2015 | NF1, NF2, SCHW | Analysis of registry data,clinic accessibility | 4617 |
| 18 | Sep 2015 | NF1 pediatric | Observational: QoL fieldtesting | 3574 |

MPNST* = Malignant Peripheral Nerve Sheath Tumor.

https://doi.org/10.1371/journal.pone.0178639.t009



Stirnadel-Farrant *et al. Orphanet Journal of Rare Diseases* (2018) 13:49
https://doi.org/10.1186/s13023-018-0791-9

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Gene therapy in rare diseases: the benefits and challenges of developing a patient-centric registry for *Strimvelis* in ADA-SCID

Heide Stirnadel-Farrant[1*], Mahesh Kudari[2], Nadia Garman[1], Jessica Imrie[3], Bikramjit Chopra[2], Stefania Giannelli[4], Michela Gabaldo[4], Ambra Corti[4], Stefano Zancan[4], Alessandro Aiuti[4,5,6], Maria Pia Cicalese[4,5], Rohit Batta[2], Jonathan Appleby[1], Mario Davinelli[7] and Pauline Ng[2]

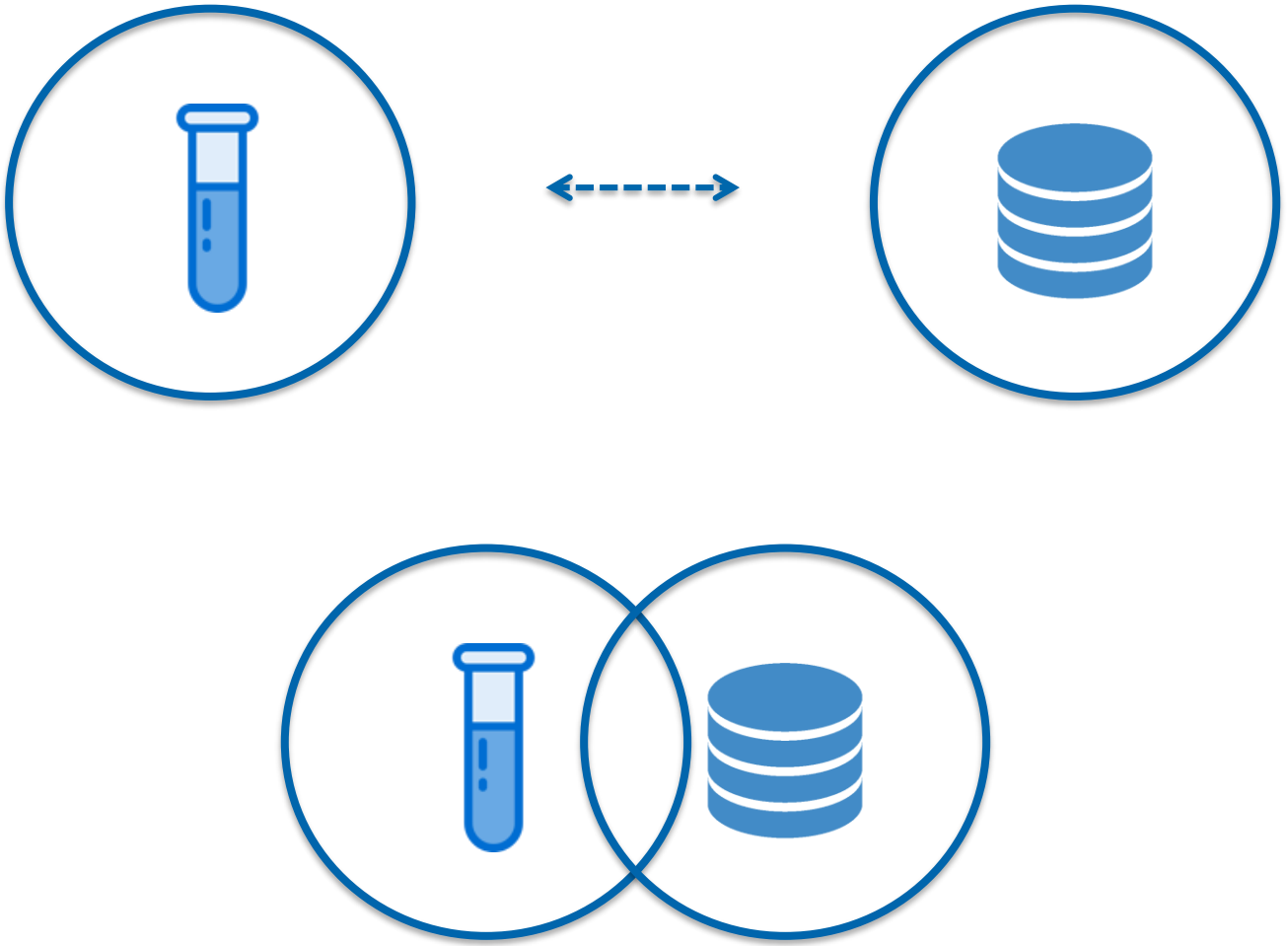
Observational registry to monitor the safety and effectiveness of Strimvelis in up to 50 patients over a minimum of 15 years, to meet the EMA's regulatory requirements of an approved gene therapy

# Similarities between registries and biobanks

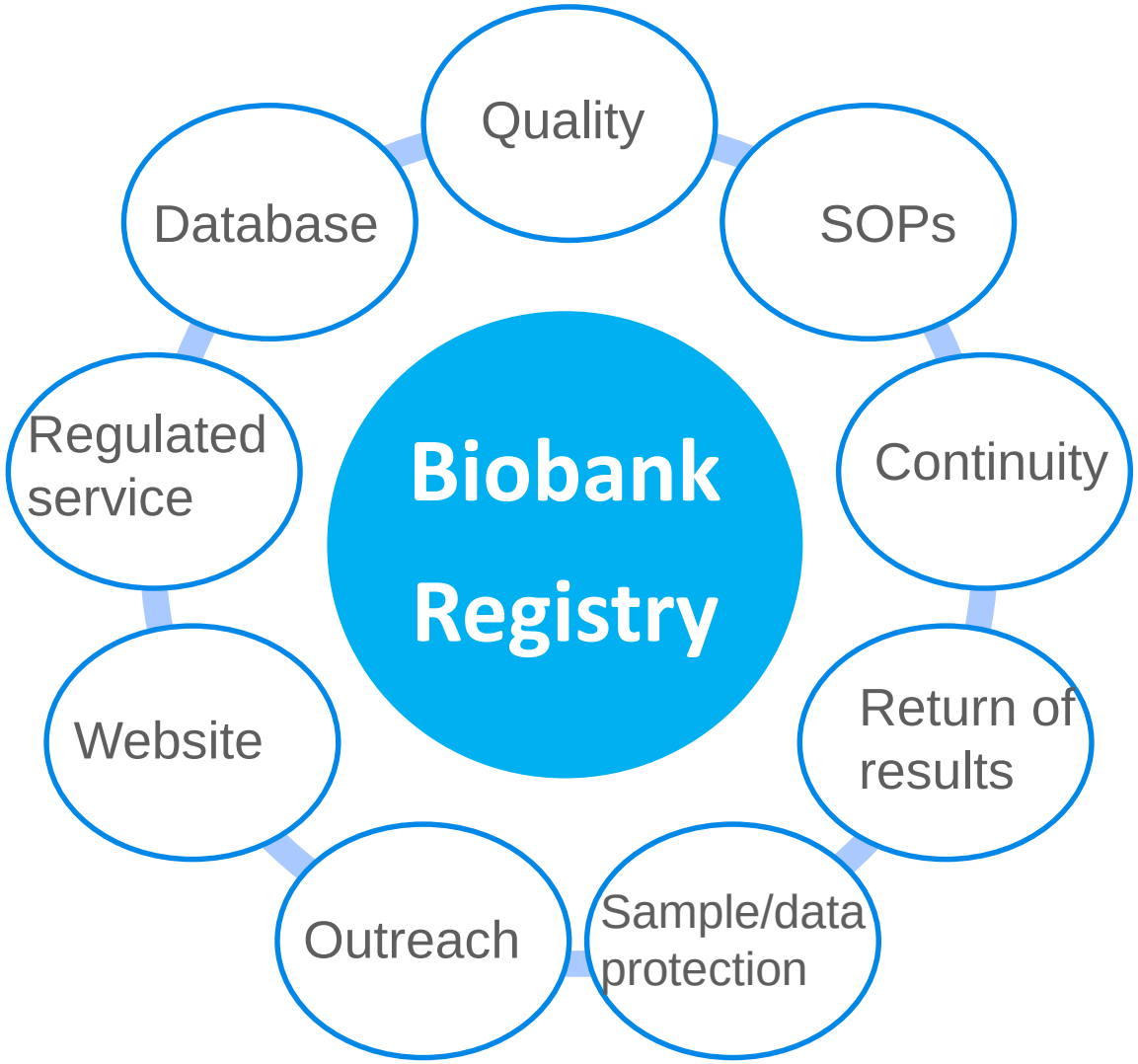
- ✓ Extremely valuable for reseach
- ✓ Collection of resources (data, biological samples)
- ✓ Require good data management and quality
- ✓ Require good governace for their operations
- ✓ Involve multiple stakeholders: patients, clinicians, reseachers
- ✓ National and international networks and standards
- ✓ Need to be sustainable

| | Biobank | Registry |
|---|---|---|
| *Main resources* | Biological samples<br>Clinical data | Quality of life<br>Clinical data<br>Medical history |
| *Supported research* | Disease mechanisms<br>Biomarker identification<br>Diagnostic tools<br>Pre-clinical tests | Natural history<br>Clinical trials & design<br>Regulatory requirements |
| *Focus* | Diseases, conditions, exposure<br>Cohorts | Diseases, conditions, exposure<br>Product |
| *Governance*<br>*stakeholders*<br>*access policy* | Yes | Yes |
| *Infomed consent* | Yes | Yes |
| *Quality standards* | Yes | Yes |
| *Data standards* | Yes | Yes |
| *MTA/DTA* | Yes | Yes |

# Opportunity



# Patient involvement




Governance of biobank/registry

Drive creation of dedicated sample collections, databases

Drive formation of networks and collaborations

Societal engagements

# Summary

**Biobanks and registries**

…are fundamental resources for research

…share many common operational features

…support complementary types of research activities

…should be interoperable

…together can create synergies

Thank you!

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FONDAZIONE Telethon