Database of shared samples through deposition at biorepositories and omics data with associated phenotypic data via submission to databases and RD-Connect.

Rare disease research area has a significant demand for the biological samples and associated phenotype and genomic information. Scarcity of the data and samples available for research purposes is well recognised obstacle on the way of translational research. RD-Connect offers a solution to this issue in a form of RD-Connect Registry and Biobank Finder tool. RD-Connect is a 6 years global infrastructure project initiated in November 2012 that links genomic data with patient registries, biobanks, and clinical bioinformatics tools to create a central research resource for RDs (1). The finder comprises aggregated up to date information on 62 000 biological samples available across 21 biobanks from more than 15 countries worldwide. The tool is easy to navigate and user friendly. The finder is also a portal to other RD-Connect tools, providing a link to the RD-Connect Sample Catalogue, a large inventory of RD biological samples available in participating biobanks for RD research.

Figure 1.Shows the overview of some of the biobanks feeding in the RD-Connect Biobank Finder tool. The number of participating organisations is constantly growing. Potential researchers can chose to use biobanks within their country or on an international level, providing the consent form allows cross border sharing of anonymised samples.

Figure 2 demonstrates navigation panel that allows to further narrow the search and chose a particular condition, tissue type and relevant phenotype or clinical information collected alongside with the sample.

Table 1 is an example of an enquiry for sample availability. The table below gives an overview of locally (Newcastle Biobank) available samples. This includes samples from a variety of diagnosed and undiagnosed patients. In total, biobank contains samples representing over 100 rare conditions. The biobank also provides a choice of tissues, cells and DNA/RNA specimens to choose from. Academical researchers (e.g. John Walton Muscular Dystrophy Research Centre) and commercial companies (e.g. Pfizer) have successfully used samples from this biobank for a biomarker research studies (2, 3) in the past.

Eurobiobank along with RD-Connect promotes further integration and interoperability between biobanks, registries and omics project in order to increase efficiency of data and samples usage (4).

Figure 1 . RD-Connect Biobank Finder tool. A snapshot of the biobank navigation panel.

Figure 2. Sample navigation tool

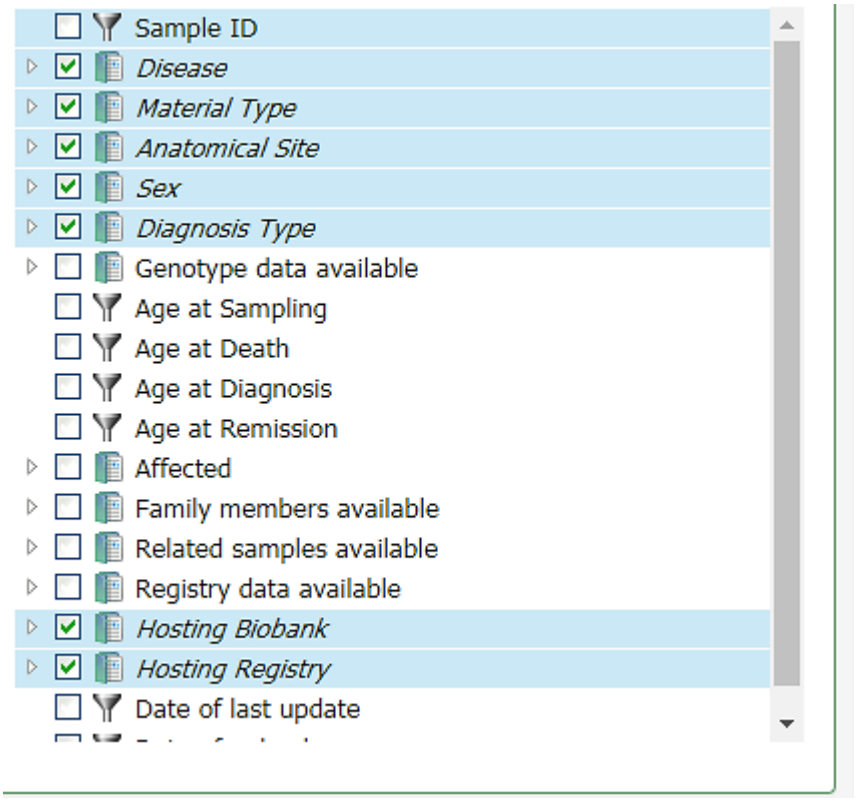

Table 1. Example of the enquiry in a local biobank (Newcastle, UK), showing available tissues and samples.

Diagnosis	Fibroblasts	Myoblasts	Plasma	Serum	Urine	DNA	RNA
ADULT-ONSET CEREBELLAR ATAXIA DUE TO CABC1/ADCK3 MUTATION	1						
AGE-RELATED MACULAR DEGENERATION	8					2	
ATYPICAL HEMOLYTIC-UREMIC SYNDROME	2						
BECKER MUSCULAR DYSTROPHY	1		59	74		59	
BECKER MUSCULAR DYSTROPHY FEMALE CARRIER			8	10		6	
BEHR SYNDROME	1						
BENIGN FASCICULATION SYNDROME		1					
BETHLEM MYOPATHY	17		17	18		17	
BLUE CONE MONOCHROMATISM	1						
CENTRAL CORE DISEASE			3	6		7	
CENTRONUCLEAR MYOPATHY				1			
CHARCOT-MARIE-TOOTH DISEASE (NOT SPECIFIED)	2						
CHARCOT-MARIE-TOOTH DISEASE, X-LINKED	2		1	1		1	
COENZYME Q10 DEFICIENCY	1	1					
CONGENITAL MYASTHENIC SYNDROMES	25	2	6	9		264	
DISTAL MYOPATHY	1		3	4		1	
DMD/BMD INTERMEDIATE	3		6	4		6	
DMD/BMD INTERMEDIATE FEMALE CARRIER			1	1			

DUCHENNE MUSCULAR DYSTROPHY	71	25	119	134	24	194	
DUCHENNE MUSCULAR DYSTROPHY FEMALE CARRIER			23	39		23	
EMERY-DREIFUSS MUSCULAR DYSTROPHY				3		2	
ENHANCED S-CONE SYNDROME	1						
FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY TYPE 2			1	52		3	
FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY			26	42		38	
FRIEDREICH ATAXIA	28					29	
HEREDITARY INCLUSION BODY MYOPATHY	18			271	195	31	
IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION		6					
INCLUSION BODY MYOPATHY WITH EARLY-ONSET PAGET DISEASE WITH OR WITHOUT FRONTOTEMPORAL DEMENTIA	7		1	7		2	
INCLUSION BODY MYOSITIS	1	1				6	
INHERITED PERIPHERAL NEUROPATHY CMT2	1						
KENNEDY DISEASE						1	
LEBER HEREDITARY OPTIC NEUROPATHY	16	1					
LEUKOENCEPHALOPATHY WITH VANISHING WHITE MATTER; VWM	1						
LIMB-GIRDLE MUSCULAR DYSTROPHY (NOT SPECIFIED)	4		1				
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 1B				3		30	

LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 1C				3			
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2L	3	1	4	15		4	
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2A	1	2	9	31		6	
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2B	75		661	656	5	213	228
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2C				4		1	
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2F	1					2	
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2I	2		1	15			
MARINESCO-SJÖGREN SYNDROME	5		2	2		6	
MELAS SYNDROME	4					5	
MERRF SYNDROME	6	1					
MITOCHONDRIAL COMPLEX I DEFICIENCY		1					
MITOCHONDRIAL COMPLEX II DEFICIENCY	1						
MITOCHONDRIAL COMPLEX III DEFICIENCY	2	1					
MITOCHONDRIAL DISORDER	12	23					
MITOCHONDRIAL MYOPATHY	3	5					
MITOCHONDRIAL NEUROGASTROINTESTINAL ENCEPHALOMYOPATHY		1					
MIYOSHI MYOPATHY	2						
MORPHEA SCLEROSIS		1					
MULTI-MINICORE MYOPATHY			1	2			
MULTIPLE SCLEROSIS		1				1	

MUSCULAR DYSTROPHY, CONGENITAL MEROSIN-DEFICIENT, 1A			1	4		2	
MYASTHENIA GRAVIS	2					2	
MYOFIBRILLAR MYOPATHY			3	11		1	
MYOTONIA CONGENITA			1	1		1	
MYOTONIC DYSTROPHY TYPE 1	99		103	887	820	965	715
MYOTONIC DYSTROPHY TYPE 2						3	
NEMALINE MYOPATHY			1	1			
NEMALINE MYOPATHY; NEM2						4	
NEUTRAL LIPID STORAGE DISEASE WITH MYOPATHY	2						
OPTIC ATROPHY	3	2					
OPTIC ATROPHY 1	4	17					
POMPE DISEASE (GLYCOGEN STORAGE DISEASE)	3	2	1	2			
PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA (POLG2)		1				1	
RETINITIS PIGMENTOSA	12						
SEVERE EARLY-ONSET AXONAL NEUROPATHY DUE TO MFN2 DEFICIENCY	2	1					
SJÖGREN SYNDROME	1	1					
SPINAL MUSCULAR ATROPHY TYPE 1	5	4					
SPINAL MUSCULAR ATROPHY TYPE 2	4		1	3		2	
SPINAL MUSCULAR ATROPHY TYPE 3	3	2				3	
SPINAL MUSCULAR ATROPHY WITH RESPIRATORY DISTRESS	1					1	
TITINOPATHY/MYOFIBRILLAR MYOPATHY			1	4		1	

ULLRICH CONGENITAL MUSCULAR DYSTROPHY	6		2	2	1	2	
WOLFRAM SYNDROME 1	8	2				2	
MULTIPLE ACYL-CoA DEHYDROGENASE DEFICIENCY	2	2					
CONTROL	19	49	3	28	14	1	
NEUROFERRITINOPATHY						5	
X-LINKED MYOTUBULAR MYOPATHY (MTM1 mutation)	1						
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2E	1						
VALOSIN-CONTAINING PROTEIN	2		1	1		2	
OCULOPHARYNGEAL MUSCULAR DYSTROPHY			1	2		5	
OCULOPHARYNGODISTAL MYOPATHY						3	
LIPID STORAGE MYOPATHY						2	
RYANODINE RECEPTOR 1 RELATED MYOPATHY			3	4		31	
MYH7 RELATED MYOPATHY			1			5	
MYOTONIC DYSTROPHY, UNSPECIFIED						2	
ADAMS OLIVER SYNDROME						2	
GNE MYOPATHY	1		1	1		1	
MOTOR PREDOMINANT AXONAL PERIPHERAL NEUROPATHY	1						
CHARCOT-MARIE-TOOTH DISEASE TYPE 1B; CMT1B	1						
JOUBERT SYNDROME	7						
CHARCOT-MARIE-TOOTH DISEASE TYPE 2D; GARS	7						
CHARCOT-MARIE-TOOTH DISEASE TYPE 2N AXONAL; AARS	4						

MENKES DISEASE	1						
HEREDITARY MYOPATHY WITH EARLY RESPIRATORY FAILURE			1	1		1	
USHER SYNDROME	1						
UNDIAGNOSED	532	612	4	4		5627	
MYOADENYLATE DEAMINASE DEFICIENCY			1	1		1	
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2H			1			1	
WELANDER DISTAL MYOPATHY			1	1		1	

Table 2. An overview of samples in the biobanks available for search in RD-CONNECT Finder tool (as of Feb 2019).

Sample type	number
Other	138
Portion of urine	1057
Skeletal muscle tissue	8457
Portion of cerebrospinal fluid	567
Set of tissues	517
Portion of saliva	24
Blood cell	5071
Leukocyte	456
T lymphocyte	325
Portion of plasma	1034
Portion of serum	7203
Fibroblast	3028
Peripheral nerve	231
RNA	2006

Myoblast	282
Pluripotent stem cell	8
Plasma cell	4517
Skin	4
Set of aminergic cells	180
Liver	2
DNA	25523
Trophoblast cell	75
Lymphoblast	969
Blood in aorta	19
Blast cell	1854
Peripheral blood cell	3
Peripheral blood mononuclear cell	119
Portion of tissue	1918
Total	65587

References:

1. Gainotti S, Torreri P, Wang CM, Reihs R, Mueller H, Heslop E, et al. The RD-Connect Registry & Biobank Finder: a tool for sharing aggregated data and metadata among rare disease researchers. European journal of human genetics : EJHG. 2018;26(5):631-43.

2. Burch PM, Pogoryelova O, Goldstein R, Bennett D, Guglieri M, Straub V, et al. Muscle-Derived Proteins as Serum Biomarkers for Monitoring Disease Progression in Three Forms of Muscular Dystrophy. Journal of neuromuscular diseases. 2015;2(3):241-55.

3. Burch PM, Pogoryelova O, Palandra J, Goldstein R, Bennett D, Fitz L, et al. Reduced serum myostatin concentrations associated with genetic muscle disease progression. Journal of neurology. 2017;264(3):541-53.

4. Mora M, Angelini C, Bignami F, Bodin AM, Crimi M, Di Donato JH, et al. The EuroBioBank Network: 10 years of hands-on experience of collaborative, transnational biobanking for rare diseases. European journal of human genetics : EJHG. 2015;23(9):1116-23.