TRANSLATIONAL RESEARCH IN RARE AND NEUROMUSCULAR DISEASES - WHY DATA SHARING MATTERS

Hanns Lochmüller, Newcastle University
Gene identification/pathophysiology

- Biomarkers
- Animal models
- Delivery mechanisms
- Proof of principle studies
Recent years have seen an increased focus on RD research, with funding opportunities from different areas.
<table>
<thead>
<tr>
<th>Project</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>TREAT-NMD</strong></td>
<td>10M EUR “network of excellence” for rare inherited neuromuscular diseases</td>
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<tr>
<td><strong>CARE-NMD</strong></td>
<td>Implementing care standards for DMD across Europe, in particular Eastern Europe</td>
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<tr>
<td><strong>Neuromics</strong></td>
<td>12M EUR research project on nextgen omics approaches to neuromuscular and neurodegenerative disease</td>
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<tr>
<td><strong>RD-Connect</strong></td>
<td>12M EUR RD infrastructure: central global hub connecting registries, biobanks and clinical bioinformatics</td>
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<tr>
<td><strong>NMD-Chip</strong></td>
<td>High throughput sequencing (gene chips) for NMD diagnostics</td>
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<td><strong>MYO-SEQ</strong></td>
<td>Exome sequencing of 1000 patients with limb girdle phenotype</td>
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<td><strong>RARE Bestpractices</strong></td>
<td>Infrastructure for best practice sharing across rare diseases</td>
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<td><strong>EUCERD Joint Action for Rare Disease</strong></td>
<td>Implementing RD policy and national plans across Europe</td>
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<td><strong>BIO-NMD</strong></td>
<td>Identifying and validating pre-clinical biomarkers for diagnostics and therapeutics</td>
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<td><strong>SKIP-NMD</strong></td>
<td>Clinical trial for morpholino antisense oligonucleotide exon skipping (53) in DMD</td>
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<td><strong>OPTIMISTIC</strong></td>
<td>Natural history and exercise therapy clinical study in myotonic dystrophy</td>
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<tr>
<td><strong>SCOPE-DMD</strong></td>
<td>Clinical trial for 2O-ME antisense oligonucleotide exon skipping (45) in DMD</td>
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<tr>
<td><strong>3Gb-TEST</strong></td>
<td>Introducing diagnostic applications of ‘3Gb-Testing’ in human genetics</td>
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<tr>
<td><strong>BIOIMAGE-NMD</strong></td>
<td>Development of imaging technologies for therapeutic interventions in rare diseases</td>
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<td><strong>MYO-MRI</strong></td>
<td>Applications of MR imaging and spectroscopy techniques in neuromuscular disease</td>
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<tr>
<td><strong>FUTURE ...</strong></td>
<td>Horizon 2020</td>
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</table>
But: risk of data silos increases
Sharing: What?

- Raw data from all types of studies
- Genomic data
- Phenotypic data
- Natural history data
- Clinical trial data
- Biosamples (blood, DNA, tissue samples, cell lines...)
- Linked data and samples
- Access to patients
- ...

RDConnect

05 March 2015
Sharing: Barriers

- **General**
  - Privacy protection issues: “do I have the patient’s permission?”
  - Lack of infrastructure: “I want to share data but where do I put it?”
  - Lack of standards and interoperability

- **Academia**
  - Culture of protecting research results: “someone else might scoop my publication!”
  - Lack of incentives for sharing

- **Industry**
  - IP issues/competition (sharing own data)
  - Concerns over data quality, regulatory compliance (reusing data from academia)
Sharing: Benefits

- Overcoming the “rare disease problem”
  - Cohort size
  - Powering trials
  - Finding confirmatory cases
- Reducing costs
- Reducing duplication of effort
- Facilitating validation of results
- Enabling engagement with experts and the patient community
Using shared biosamples: Infrastructure – the MRC biobank

- MRC biobank established at 2 sites (Newcastle and London)
- Full member of EuroBioBank network and open catalogue
- More than 5000 NMD samples collected so far
- More than 100 different neuromuscular pathologies
- Samples distributed to more than 100 scientists (centre and external)
- More than 50 research publications acknowledging biobank
- Several successful grant proposals with strong biobank element
Using patient cells to validate experimental therapies:
Neutral Lipid Storage Myopathy due to PNPLA2 mutations

Recessive inheritance
Adult onset myopathy
Cardiomyopathy
Jordan bodies

Clenbuterol may be an attractive candidate for testing in animal models (R Horvath)
Sharing: example projects
Patient registries:
DMD registries pre-TREAT-NMD (2007)
Patient registries: DMD registries today (2015)

> 10,000 patients in 35+ countries – global data for multicentre trials
Patient registries as a tool for research

- Trial readiness (feasibility and recruitment)
- Standards of care – CARE-NMD
- Biomarker discovery and validation – BIO-NMD
- Burden of illness (health economics)
- Natural history
Exon skipping – gene and mutation specific therapy for Duchenne
### DMD exon skipping – cumulative data from registries for trial feasibility

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</table>
DMD exon skipping: trial feasibility and recruitment

Yellow pins: German and Austrian trial sites (16)

Blue pins: DMD & BMD patients in German/Austrian patient registry (693)

May 2010
DMD exon skipping: trial feasibility and recruitment

Yellow pins: German and Austrian trial sites

Green pins: Patients meeting basic inclusion criteria for trial (67)

Red circle: Under the care of Freiburg (4) and Essen (9)

Blue circle: Recruitment potential (within 2 hours reach) Freiburg (15) and Essen (15)
Sharing: example projects: Infrastructure for RD data sharing
Infrastructure for RD data sharing
RD-Connect

An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research

**Overarching objectives:**

- Contribution to the IRDiRC objectives of delivering 200 new therapies for rare diseases and means to diagnose most rare diseases by the year 2020

- Development of an integrated, quality-assured and comprehensive platform in which complete clinical profiles are combined with -omics data and sample availability for rare disease research, in particular IRDiRC-funded research.
Infrastructure for RD data sharing
Data flow within RD-Connect

- Source data
  - Biomaterial data
  - Other IRDiRC project data
  - Phenotype and registry data
  - NeurOmics omics data
  - EURenOmics omics data

- Secure, permanent raw data archive
  - European Genome-phenome Archive

- RD-Connect platform
  - Combined repository for linked data
  - Directly integrated bioinformatics tools
  - Access to additional tools via webservices/APIs
Collaboration and data sharing are even more crucial in rare disease than common

Opportunities arising from the increase in RD research will be missed if projects do not share data

For large datasets (omics data), publications are not enough: raw data access is essential

Number of projects (both academic and PPP) that have been made possible as a result of sharing are proof that hurdles can be overcome

Requires a change in mindset on all sides

Requires explicit policies and incentivisation

Requires appropriate infrastructure