Networking towards clinical application of antisense-mediated exon skipping in rare diseases

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COST Domain - Biomedicine and Molecular Biosciences (BMBS)

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Splice modulation therapy approach

Disease	Stage	Mechanism
Duchenne muscular dystrophy	Phase II & III trials	Reading frame restoration
Spinal muscular atrophy	Phase I trial	Exon inclusion
β-thallassemia	Mouse model	Blocking cryptic splicing
Hutchinson-Gilford progeria	Mouse model	Isoform switching
Fukuyama congenital muscular dystrophy	Mouse model	Skip retrotransposon
Menkes disease	Zebrafish model	Blocking cryptic splicing
Atherosclerosis	Mouse model	Reading frame disruption
Limb-Girdle muscular dystrophy 2B	Mouse model	Reading frame restoration
Muscle wasting diseases	Mouse model	Reading frame disruption
Cancer	Mouse model	Isoform switching
CADASIL	Cell cultures	Cysteine quantity correction
Huntington Disease	Cell cultures	Protein modification
Spinalcerebellar ataxias	Cell cultures	Protein modification
Leber congenital amourosis	Cell cultures	Blocking cryptic splicing
Methalmalonic/Propionic acidemia	Cell cultures	Blocking cryptic splicing

Current Challenges splicing modulation

- Personalized medicine approach
  - (Subsets of) rare diseases
  - Limited patient population
- Regulatory models unfit for RDs
- Harmonization of research needed
  - Within an RD
  - Between RDs
- Jointly overcome hurdles and face challenges

COST Action BM1207

Networking towards clinical application of antisense-mediated exon skipping

Involving all key stakeholders (clinicians, scientists, industry, **patients** & regulators)

- Facilitate the clinical development of antisense-mediated exon skipping for rare diseases
- Exploit exon skipping for as many patients as possible

Objectives

1. Achieve consensus biochemical outcome measures
2. New regulatory models to allow testing of personalized medicine approaches
3. Foster synergistic work (workshops and key stakeholder meetings and exchange visits)
4. Address therapeutic misconception by training early stage researchers

Current parties involved: Belgium, Cyprus, Denmark, Estonia, France, Germany, Greece, Israel, Italy, Malta, Netherlands, Norway, Portugal, Romania, Serbia, Spain, Sweden and United Kingdom

If you are interested to join, please contact the Chair of this Action

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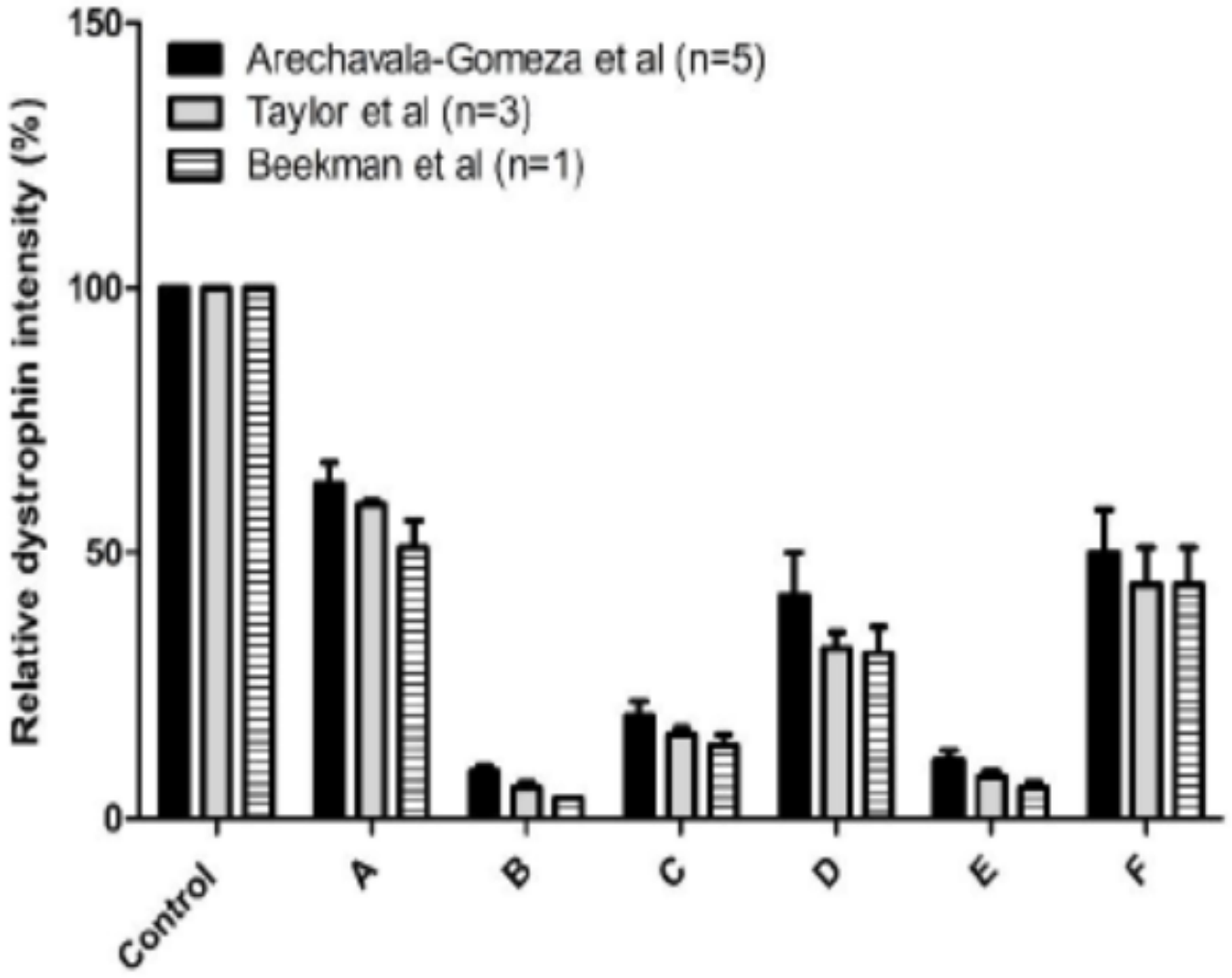
Achievements BOM working group



Achievements RM working group

- Train regulators about DMD and exon skipping
- Train Academics about regulatory models
  - Express training school

Achievements RM working group

Available online at www.sciencedirect.com

ScienceDirect

Neuromuscular Disorders 25 (2015) 96–105

www.elsevier.com/locate/nmd

Workshop report

Measuring clinical effectiveness of medicinal products for the treatment of Duchenne muscular dystrophy

Stephen Lynn [a], Annemieke Aartsma-Rus [a,b], Kate Bushby [a], Pat Furlong [c], Nathalie Goemans [d], Annamaria De Luca [e], Anna Mayhew [a], Craig McDonald [f], Eugenio Mercuri [g], Francesco Muntoni [h], Marita Pohlschmidt [i], Jan Verschuuren [b], Thomas Voit [j], Elizabeth Vroom [k], Dominic J. Wells [l], Volker Straub [a,*]

Achievements RM working group

HUMAN GENE THERAPY 25:885–892 (October 2014)

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Translational and Regulatory Challenges for Exon Skipping Therapies

Annemieke Aartsma-Rus,[1,2] Alessandra Ferlini,[3] Nathalie Goemans,[4] Anna M.G. Pasmooij,[5,6] Dominic J. Wells,[7] Katerine Bushby,[2] Elizabeth Vroom,[8] and Pavel Balabanov[9]

Achievements RM working group

- Stakeholder meeting April 29, hosted by EMA, co-organized with SCOPE-DMD
- Aim
  - Discuss data collected by the field
  - Assist drafting of guidelines
  - Plan for the future
  -
  - Briefing document published on website
  - Meeting report being drafted
  - Meeting was streamed, recording will be made available (link published on website)

Achievements Working Group 3

- Exchanges visits young researchers
  - 13 so far!
- Joint workshops on common challenges
  - Delivery
  - Delivery to CNS
  - Regulatory challenges
  - Animal models
  - (Delivery and delivery to CNS)

Stakeholder communication

- Website (www.exonskipping.eu)
- Publication lay summaries of meetings/reports

- Training school to teach early stage researchers in communicating work and results to patient community in a clear and unbiased way
- Collaboration with behavioural scientists and patient representatives
- 23-25 April in Leiden
- Big success; trainees and trainers learned a lot
- Evaluation pending

Thank you