ASX ANNOUNCEMENT

BENITEC BIOPHARMA LIMITED (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW)

23 September 2015

BENITEC FEATURED AT CHI'S "DISCOVERY ON TARGET" CONFERENCE

Dr. Peter French Leads Discussion on Gene Silencing/Gene Therapy Approaches

Sydney, Australia: Benitec Biopharma (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW), a clinical-stage biotechnology company developing innovative therapeutics based on its gene silencing technology, DNA-directed RNA interference (ddRNAi), today announced that Peter French, Ph.D., the Company's CEO and Managing Director, was invited to discuss Benitec's ddRNAi technology at The Cambridge Healthtech Institute's (CHI) 13th Annual Discovery on Target Conference in Boston, MA.

Dr. French chaired part of the *Gene Therapy Breakthroughs* session titled, "*Combining Gene Silencing/Editing and Gene Therapy*", where he discussed Benitec's core ddRNAi approach, which combines the specificity of gene therapy vectors with the power of RNA interference to produce novel 'single shot' therapies for serious life threatening diseases. The other speakers in this session included professionals from leading medical and academic institutions.

Benitec was also featured during the Conference's symposium on *Strategies for Rare Diseases; Update on Scientific Breakthroughs and Novel Approaches*, where Dr. French provided an overview of the Company's novel gene silencing and replacement program for treating Oculopharyngeal Muscular Dystrophy (OPMD). OPMD is a late-onset degenerative muscle disorder caused by a mutation in the PABPN1 gene. It is an orphan disease with an estimated prevalence of one in 100,000 people (Europe). Dr. French described Benitec's approach to treating OPMD, which uses ddRNAi technology to simultaneously silence the mutant PABPN1 gene and insert a normal copy of the gene. Benitec has achieved *in vivo* proof of concept and is planning to advance this program to human clinical studies.

Dr. French stated, "We appreciate the opportunity to highlight our achievements in this field, and thank CHI and the organizers of this conference for inviting us to participate and lead this important discussion. As we continue to validate our approach by advancing our lead clinical program, TT-034 for treating hepatitis C, we are proud to be part of the ongoing scientific dialogue that will help drive further innovation in gene therapy."

More information on CHI's Discovery conference can be found at www.discoveryontarget.com.

For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at www.benitec.com.

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About Benitec Biopharma Limited:

Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) is a clinical-stage biotechnology company developing innovative therapeutics based on its patented gene-silencing technology called ddRNAi or 'expressed RNAi'. Based in Sydney, Australia with labs in Hayward, CA (USA) and collaborators and licensees around the world, the company is developing ddRNAi-based therapeutics for chronic and life-threatening human conditions including hepatitis C and B, wet age-related macular degeneration and OPMD. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain and retinitis pigmentosa.

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silencing genes for life™

ddRNAi and Gene Replacement for Oculopharyngeal Muscular Dystrophy (OPMD)

Dr. Peter French, CEO
Benitec Biopharma

Prof George Dickson,
Royal Holloway University of London
Dr Capucine Trollet,
Institut de Myologie, Paris

Forward Looking Statements

Today's presentation includes forward-looking statements intended to qualify for the Safe Harbor from liability established by the Private Securities Litigation Reform Act of 1995. These forward-looking statements, including statements regarding our planned pre-clinical studies and clinical trials, regulatory approval process and demand for our product candidates, are subject to risks, uncertainties and other factors that could cause actual results to differ materially from those suggested by our forward-looking statements.

These factors include, but are not limited to, the following: we have incurred significant net losses and anticipate that we will continue to incur significant net losses for the foreseeable future; we have never generated any revenue from product sales and may never be profitable; we will need to raise additional funding in the future, which may not be available on acceptable terms, or at all; no product candidates utilizing ddRNAi technology have been approved for commercial sale in the United States, and our approach to the development of ddRNAi technology may not result in safe, effective or marketable products; we are early in our product development efforts and may not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates; our ability to develop and successfully commercialize product candidates may be compromised by other companies developing their technologies or product candidates for our target indications more rapidly than we do or if their technologies are more effective; we may not be able to obtain exclusivity or intellectual property rights for our product candidates or prevent others from developing similar competitive products; issues may arise that impact ddRNAi delivery into the cells and limit our ability to develop and commercialize product candidates.

This presentation is for information purposes only and does not constitute an offer to sell, or a solicitation of an offer to buy, any securities in any jurisdiction. The distribution of this presentation in jurisdictions outside Australia may be restricted by law and any such restrictions should be observed. Any failure to comply with such restrictions may violate application securities laws.

About Benitec Biopharma

Public company (Dual listed):

- ASX: BLT
- NASDAQ: BNTC

Technology: DNA-directed RNAi

- Developed at CSIRO (Australia)
- RNAi delivered with gene therapy vectors
- Long term gene silencing from a single administration
- Global patents on platform and specific applications

Pipeline programs:

- Clinical: hepatitis C (US trial sites)
- Preclinical: hepatitis B, wet and dry AMD, oculopharyngeal muscular dystrophy
- Multiple sublicenses: AIDS, Huntington's, retinitis pigmentosa, neuropathic pain, cancer

Corporate office: Sydney, Australia

Research facility: San Francisco, USA

Staff: 24

Clinical features of OPMD

Rare autosomal dominant inheritance

- 1:100,000 (Europe)
- As high as 1:600 in specific populations
- Founder effect in Quebec, Canada

Typically onset occurs in the fifth to early sixth decade of life

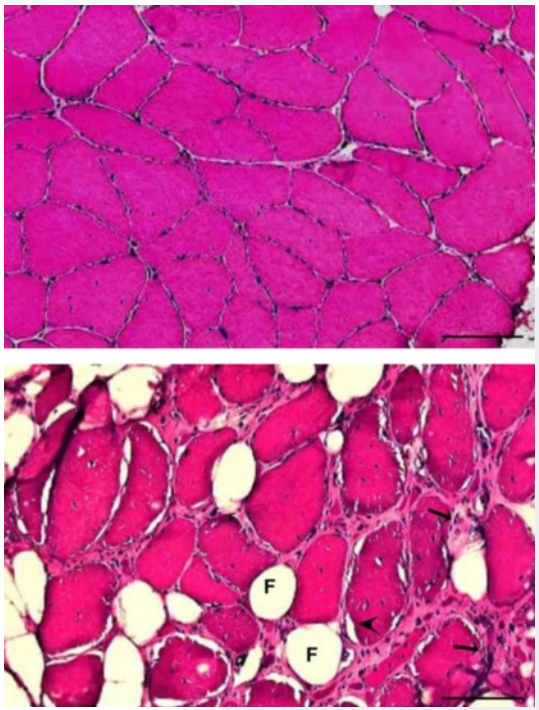
Characterised by:

- eyelid drooping (ptosis)
- swallowing difficulty (dysphagia)
- proximal limb weakness
- death due to aspiration pneumonia & malnutrition

Histopathology

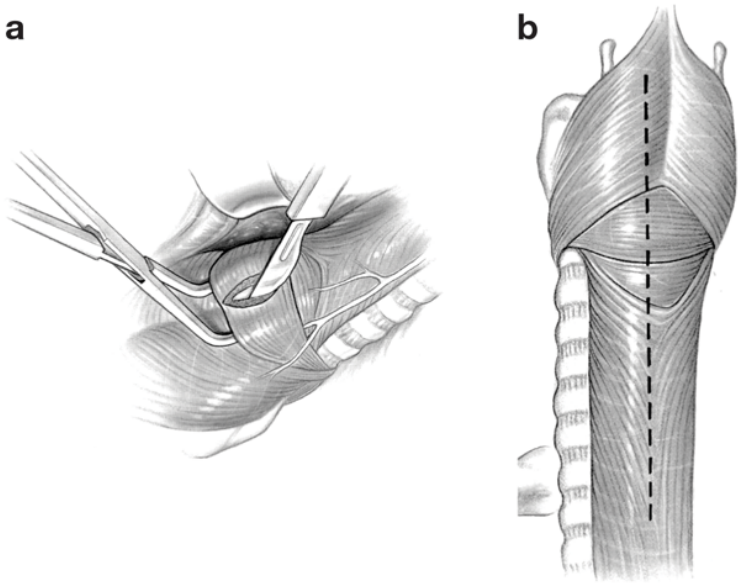
- Decrease of muscle fibre number
- Variation in the size of muscle fibres
- Infiltration (inflammatory cells)
- Fibrosis (connective tissue)

Raz et al., *BMC Neurology* 2013, **13**:70



Current treatment

Cricopharyngeal myotomy - a surgical intervention to improve swallowing but does not correct the progression of the disease since it has a genetic basis.



a: Incision of cricopharyngeus muscle.
b: Posterior view of pharynx, esophagus, and trachea. Length of myotomy is indicated by dotted line.

Chu & Kelly *GI Motility online* (2006)

Genetic basis of OPMD: expansion of the poly-alanine tract within PABPN1

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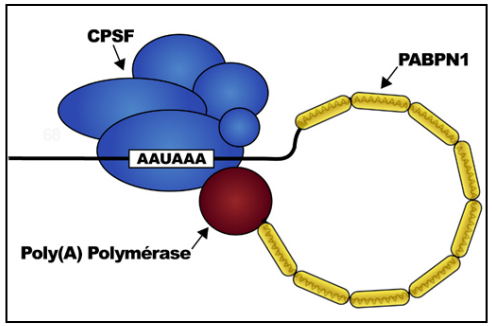
PABPN1:

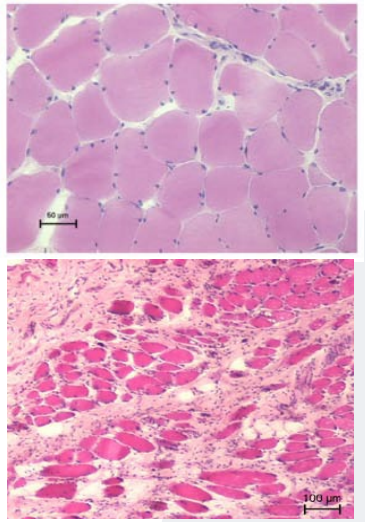
- a ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor) and thus controls the length of mRNA poly(A) tails, mRNA export from the nucleus, and alternative poly(A) site usage.



In OPMD:

- a genetic mutation results in trinucleotide repeat expansion within exon 1 of PABPN1 and results in an expanded poly-alanine tract at the N-terminal end of PABPN1.

WT ATG $(GCG)_6$ ----------$(GCA)_3$ GCG GGG GCT GCG..
MUT ATG $(GCG)_6$ $(GCG)_{1-7}$ $(GCA)_3$ GCG GGG GCT GCG…--



Non-affected

Affected

INIs, the hallmark of OPMD

Expansion of the short (GCG) trinucleotide repeat
in the coding sequence of PABPN1

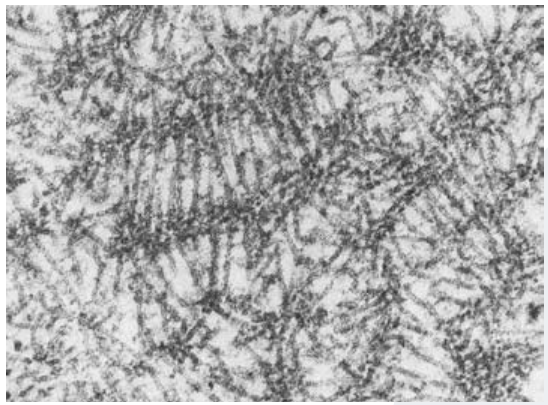
↓

The mutated protein has 11-17 alanines in the N-Terminal domain instead of 10

↓

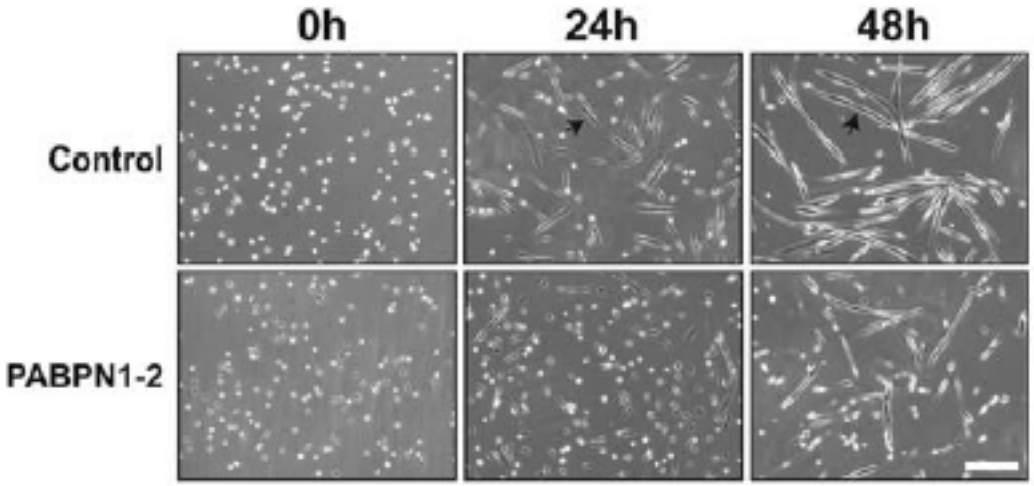
Protein aggregation forms intranuclear inclusions (INIs)

- Tubular filaments
- Resistant to degradation
- INIs found in the nuclei of skeletal muscle fibres (both affected and non-affected)



Tomé & Fardeau, 1980

A disease that is more than nuclear aggregation: PABPN1 is required to maintain muscle function



Human Molecular Genetics, 2010, Vol. 19, No. 6 **1058–1065**
doi:10.1093/hmg/ddp569
Advance Access published on December 24, 2009

Loss of nuclear poly(A)-binding protein 1 causes defects in myogenesis and mRNA biogenesis

Luciano H. Apponi[1], Sara W. Leung[2], Kathryn R. Williams[1], Sandro R. Valentini[3], Anita H. Corbett[2,*] and Grace K. Pavlath[1,*]

- PABPN1 is required for normal myoblast proliferation and differentiation
- PABPN1 is required for proper polyadenylation in muscle cells
- PABPN1 is required for proper poly(A) RNA export from the nucleus

Thus, an effective treatment likely requires maintaining endogenous function in addition to eliminating mutant protein aggregates

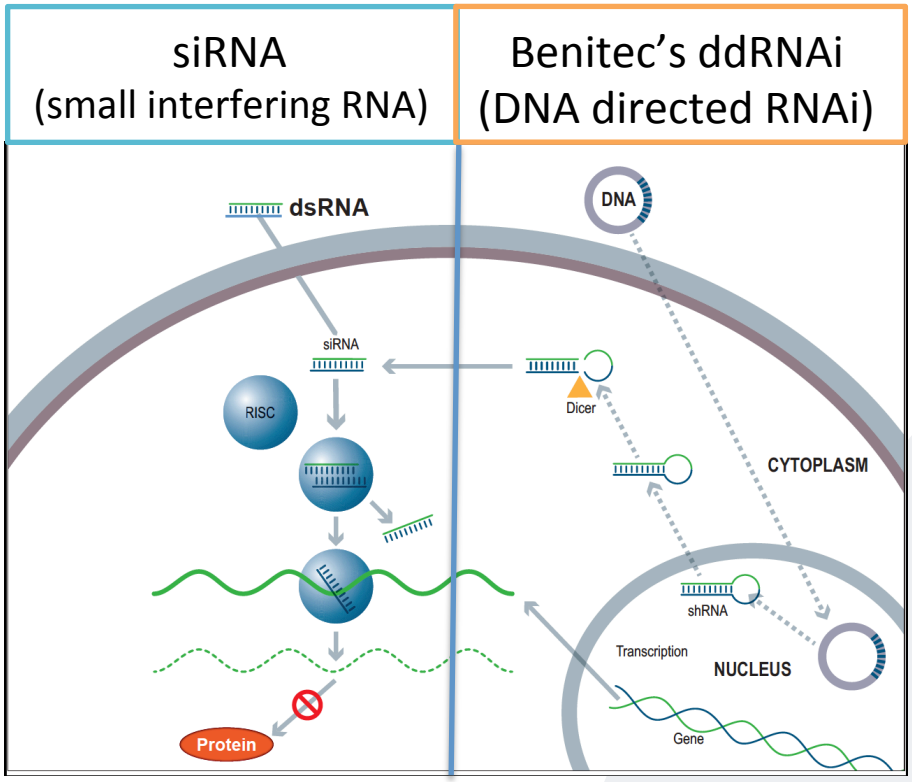
Development of a ddRNAi therapeutic for OPMD

ddRNAi: Gene Silencing Delivered with Gene Therapy Vectors

Combines RNA interference with gene therapy

- Specific delivery to target organs
- Lasting benefits from a single treatment
- Potential for multiple hairpins from a single construct – to target multiple sites on a single gene or simultaneously silence multiple genes

Protected by an **international patent estate** covering ddRNAi, specific disease targets and product candidates



Therapeutic advantages of ddRNAi

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Multi-targeting:

- Ability to target multiple genes or multiple sites on the same gene with one therapeutic construct
- Accepted by regulators as a single entity despite multi-targeting

Delivery via gene therapy vectors:

- Flexible: can use plasmids, minicircles, and potentially other approaches (stem cells, nanoparticles)
- Well established, clinically-validated systems
- Tissue specificity established by using viral vectors and pol II promoters
- Can control expression using tunable promoters

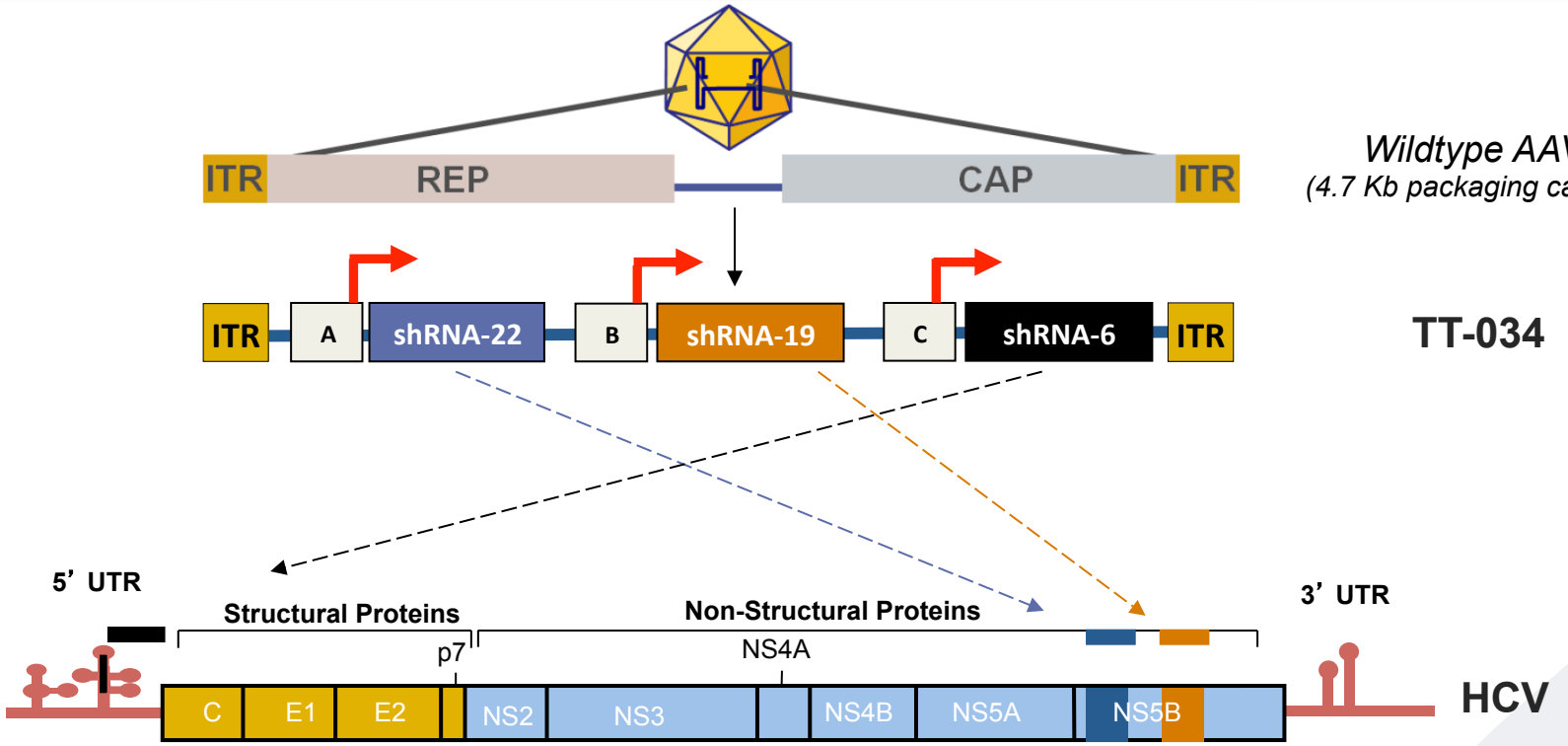
Durability of effect:

- A single treatment can produce months or years of therapeutic benefit - eliminating patient compliance issues

Enhanced safety profile:

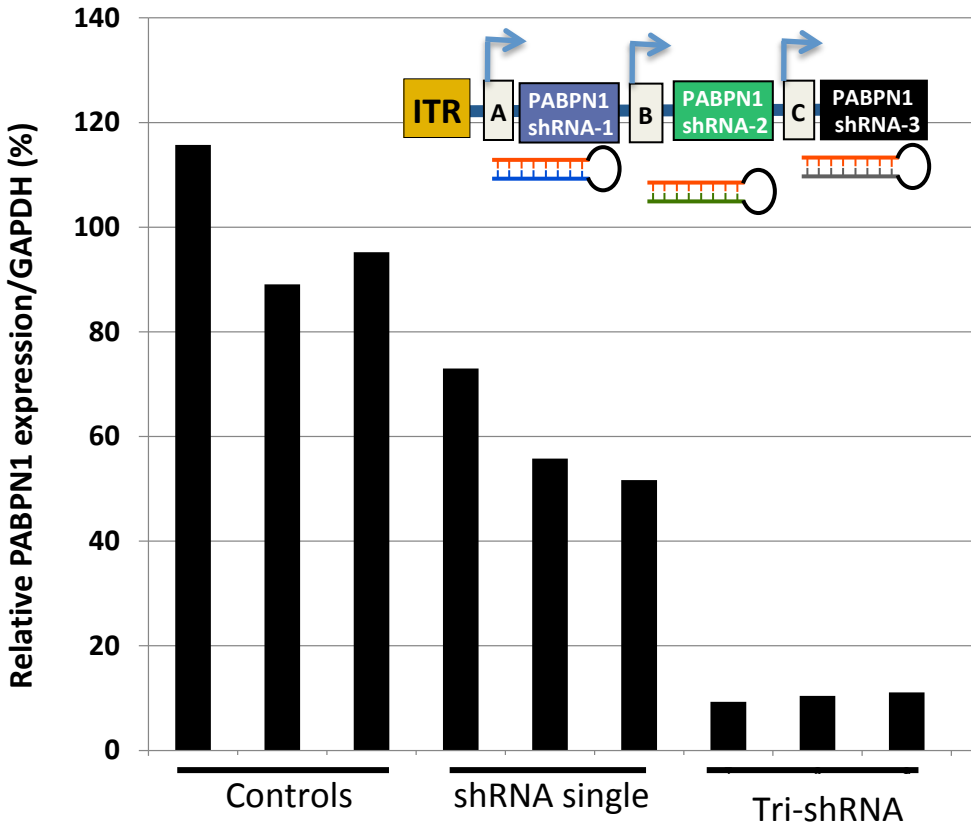
- Well understood tox profile
- Ability to use tissue-specific or cell-specific promoters
- Ability to control level of shRNA expression
- Avoids interferon activation through Toll-Like Receptors

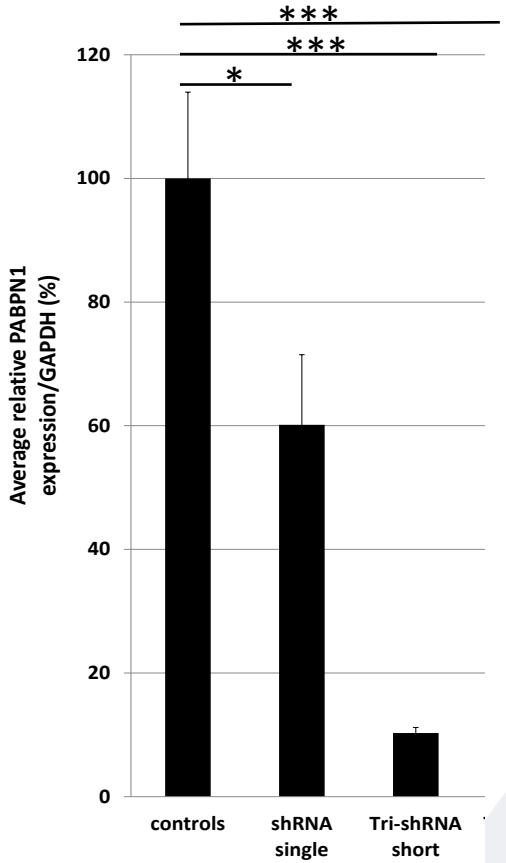
TT-034: Multiple therapeutic agents from a single vector



- Three independently transcribed RNAi elements target three separate, well-conserved regions of the HCV genome; helps prevent the generation of viral escape mutants
- Delivered with AAV8 intravenously

Use of multi-targeting properties of ddRNAi knockdown of PABPN1 in a 293T cell line

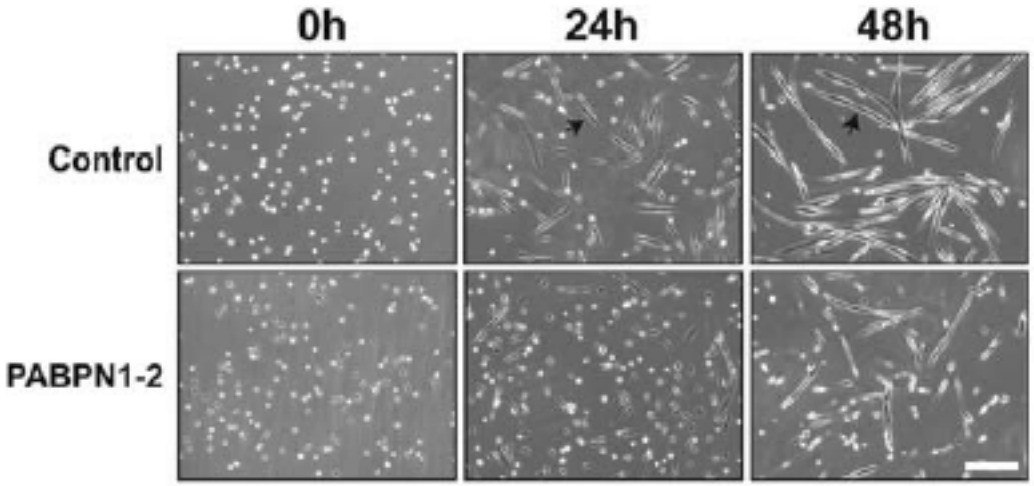




~ 90% knockdown of mutant PABPN1

G. Dickson,
personal communication

A disease that is more than nuclear aggregation: PABPN1 is required to maintain muscle function



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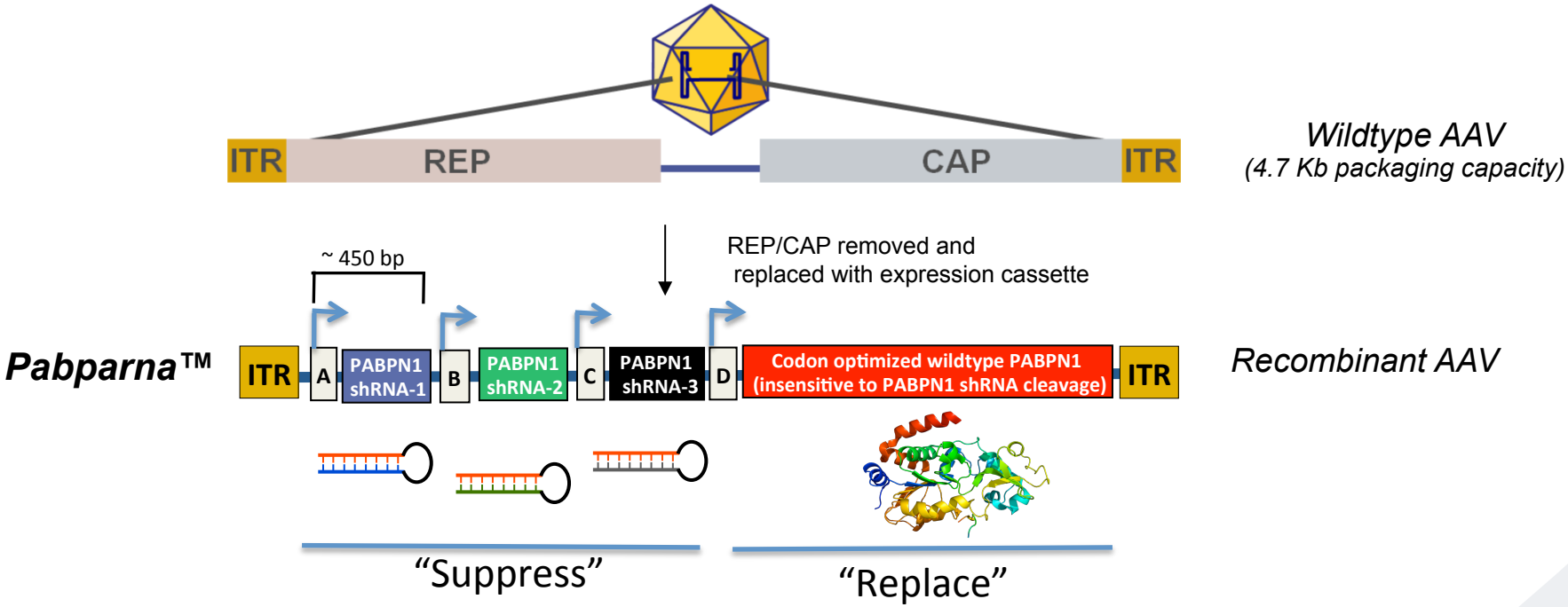
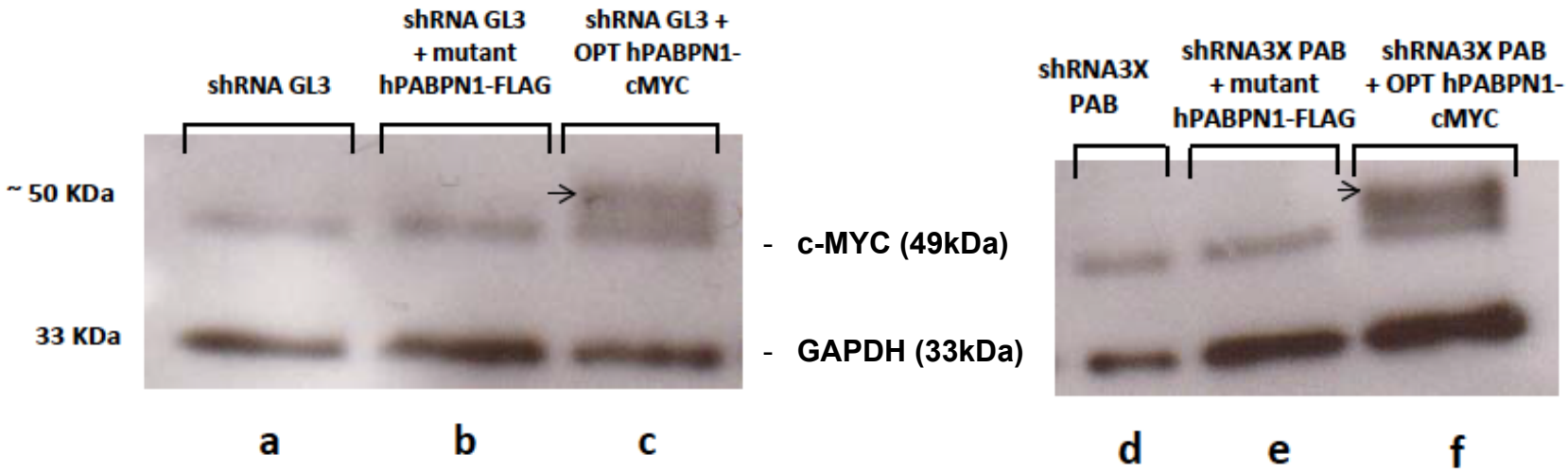
Pabparna™: A 'Suppress and Replace' approach delivered by a viral vector



- Non-integrating, non-pathogenic viral delivery system
- To date, AAV has been used in 117 clinical trials with excellent safety record
- Sustained expression (years) following single injection

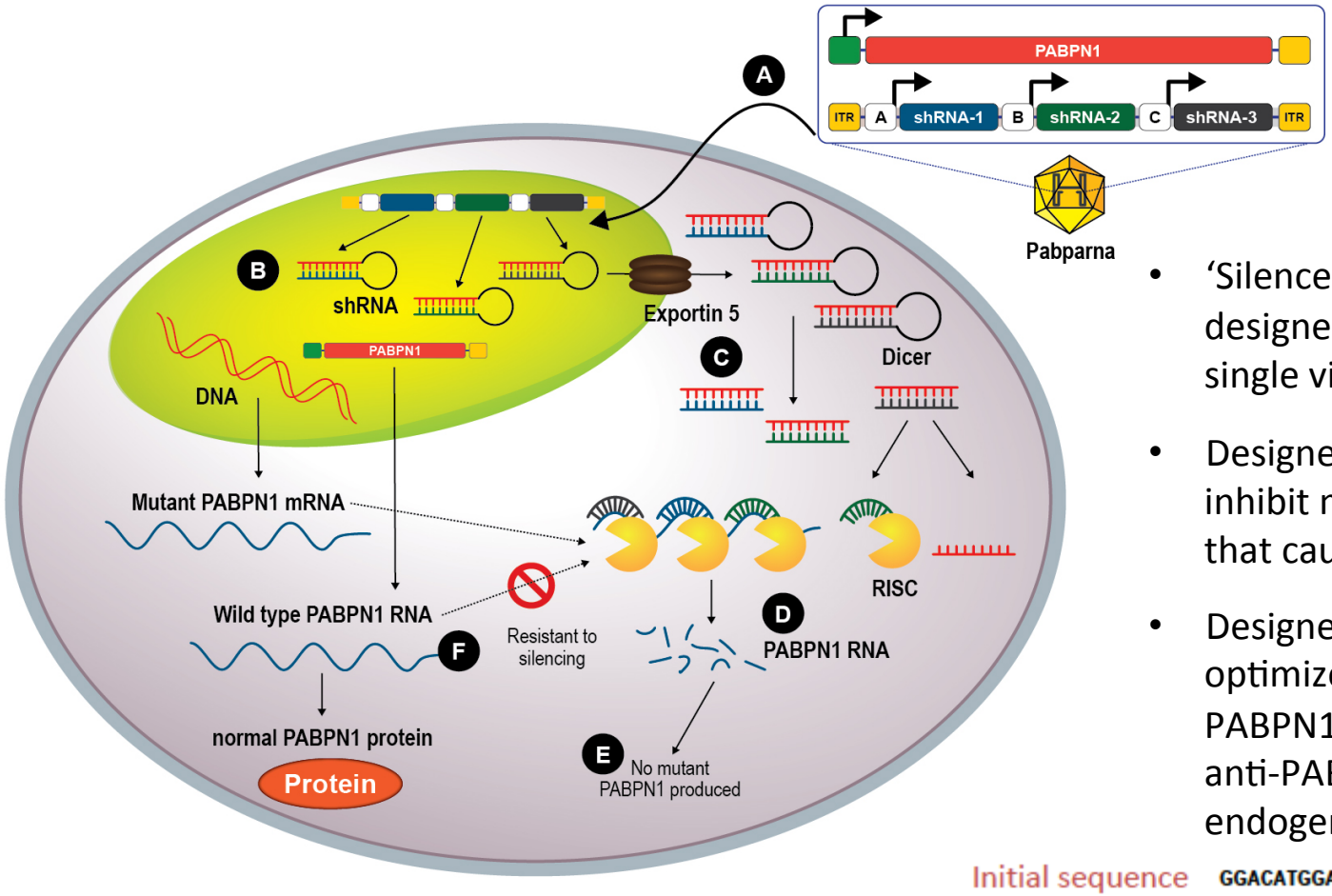
* http://www.abedia.com/wiley/vectors.php

Expression of “codon optimized” wildtype PABPN1 *in vitro*



Initial sequence	GGACATGGA GGAA GAA GC TGAGAAGCTAA AGGAG CTAC…
Codon-modified	GGACATGGAAGAGGAGGCCGAAAAACTAACGGAGTTAC…

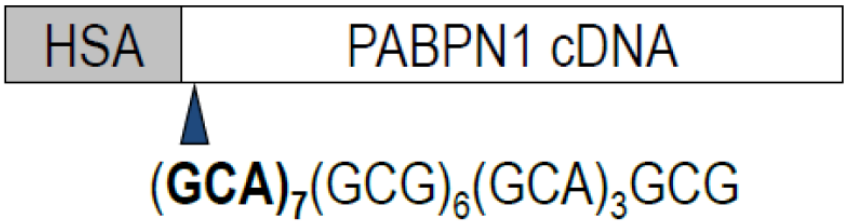
RNAi mechanism of action for Pabparna™: Our Treatment for Oculopharyngeal Muscular Dystrophy



- 'Silence and Replace' expression designed to be delivered via a single viral vector
- Designed to knock down or inhibit mutant form of PABPN1 that causes protein aggregation
- Designed to co-express a 'codon optimized' version of wildtype PABPN1 that is insensitive to the anti-PABPN1 shRNA and restores endogenous PABPN1 function

Initial sequence	GGACATGGA GGAA GAA GC TGAGAAGCTAA AGGAG CTAC...
Codon-modified	GGACATGGAAGAGGAGGCCGAAAAACTAACGGAGTTAC...

An animal model of OPMD: The 'A17' mouse



Knock-in mouse created with insertion of a mutated bovine PABPN1 driven by the human skeletal actin promoter

Recapitulates severe muscle atrophy

Mimics many of the disease pathologies:

- Progressive muscle weakness/ Atrophy
- Infiltration/ Chronic Inflammation/ Fibrosis
- Mitochondrial / Ubiquitin-Proteasome defects
- Affected and non-affected muscles contain intranuclear inclusions

Human Molecular Genetics, 2010, Vol. 19, No. 11 **2191–2207**
doi:10.1093/hmg/ddq098
Advance Access published on March 5, 2010

Molecular and phenotypic characterization of a mouse model of oculopharyngeal muscular dystrophy reveals severe muscular atrophy restricted to fast glycolytic fibres

Capucine Trollet[1,2,3,4], Seyed Yahya Anvar[5], Andrea Venema[5], Iain P. Hargreaves[6], Keith Foster[1], Alban Vignaud[2,3,4], Arnaud Ferry[2,3,4], Elisa Negroni[2,3,4], Christophe Hourde[2,3,4], Martin A. Baraibar[7], Peter A.C. 't Hoen[5], Janet E. Davies[8], David C. Rubinsztein[8], Simon J. Heales[6], Vincent Mouly[2,3,4], Silvère M. van der Maarel[5], Gillian Butler-Browne[2,3,4], Vered Raz[5] and George Dickson[1,*]

Letter

Nature Medicine **11**, 672 - 677 (2005)
Published online: 1 May 2005 | doi:10.1038/nm1242

Doxycycline attenuates and delays toxicity of the oculopharyngeal muscular dystrophy mutation in transgenic mice

Janet E Davies[1], Lin Wang[1], Lourdes Garcia-Oroz[1], Lynnette J Cook[1], Coralie Vacher[1], Dominic G O'Donovan[2] & David C Rubinsztein[1]

Pathological phenotype of the A17 mouse model

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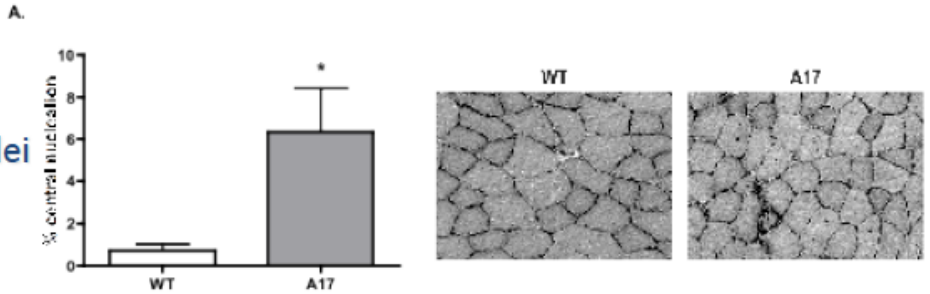
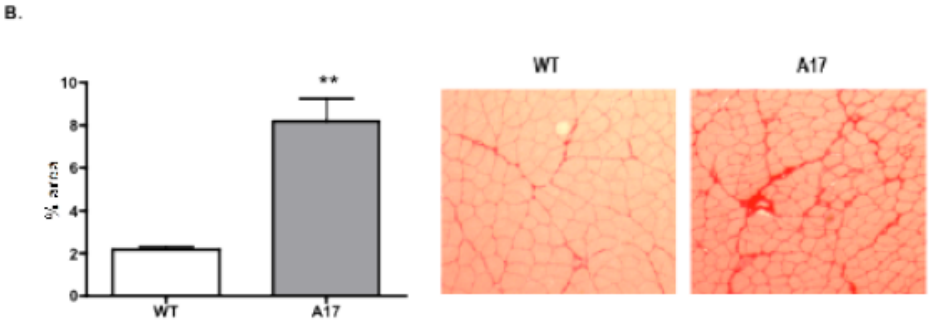
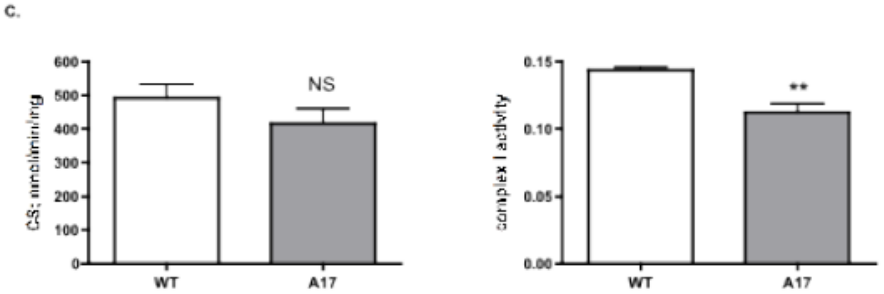
Centrally located nuclei



fibrosis



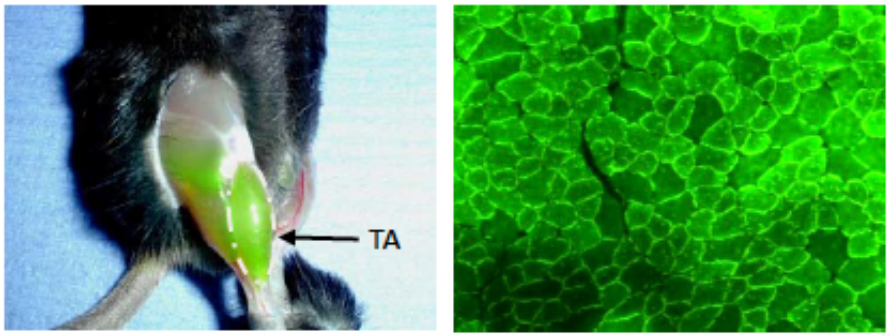
Mitochondrial Defects



In vivo delivery: AAV-GFP administered via local IM injections

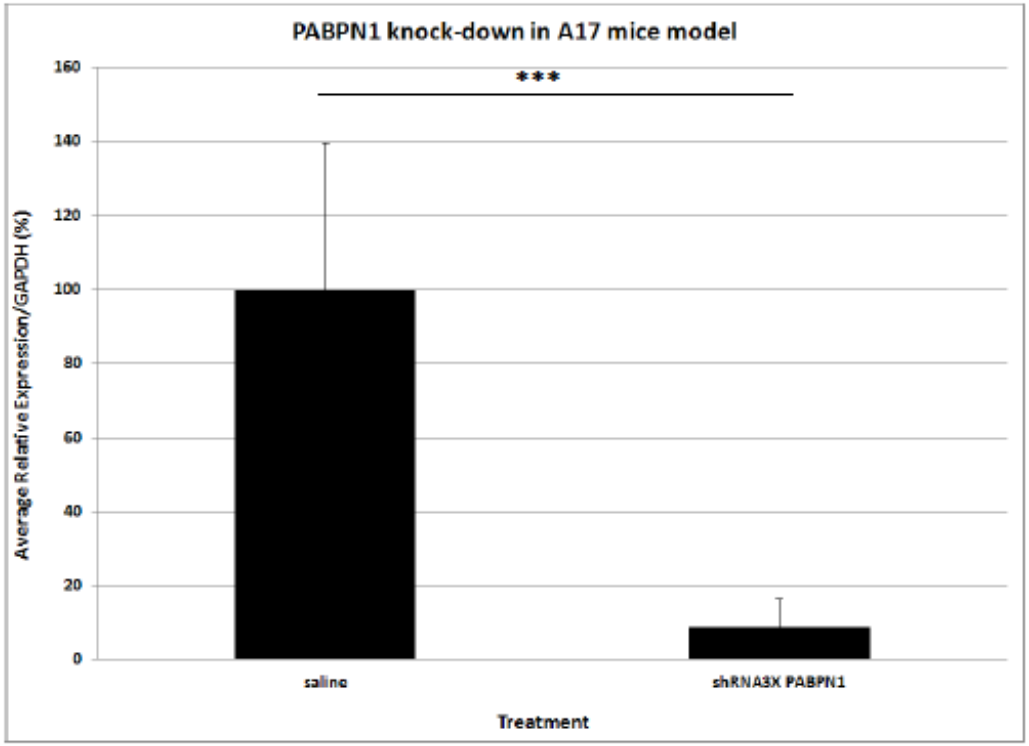
- AAV-based shRNA vector

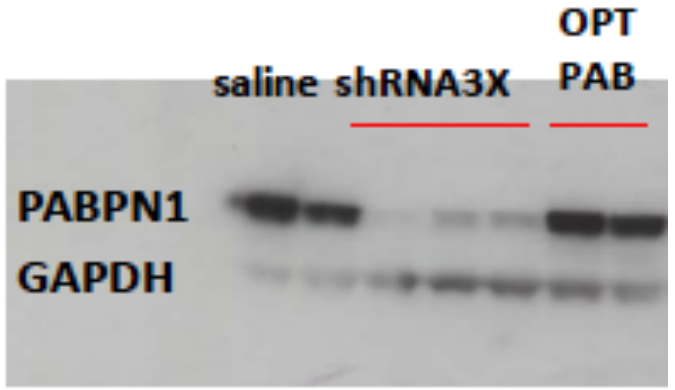
Detectable by GFP expression microscopically as early as 9 days after injection and macroscopically by 2 weeks after injection. This high level of GFP expression was maintained throughout the 56 weeks of the experiment, indicative of the presence of functional expression cassettes in myofibres.



rAAV2/6 shDys 2.10E9vg per TA muscle: 56 weeks after injection (from Mehdi Seno)

In vivo knockdown of mutant PABPN1 + expression of a "codon optimized" wildtype PABPN1 in A17 mouse





"Suppress" "Replace"

NEXT STEPS: Examining the effects of Pabparna on the phenotypes in the A17 Model system

Preliminary data to date

IN VITRO:

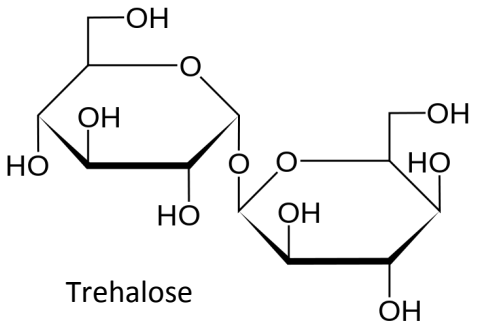
- Triple shRNA AAV construct targets mutant PABPN1.
- Efficiently ddRNAi (up to 90% KD) *in vitro & in vivo.*
- Codon-optimised PABPN1 resistant to ddRNAi / shRNA.
- Restoration of expression of normal PABPN1.

IN VIVO - Mutant PABPN1 knock-down ± replacement in A17 mouse.

- Triple shRNA AAV construct abolishes INIs but induces muscle degeneration. This can be rescued by expressing human codon-optimised PABPN1.
- Muscle mass is not restored over 4 months treatment.
- Overall muscle strength is greatly improved.
- Specific muscle strength is normalised.

Other therapies under development

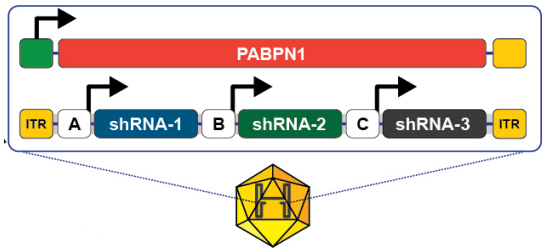
- **Trehalose**. BioBlast is in late stage clinical testing of Cabaletta, a chemical chaperone that prevents pathological aggregation of proteins within cells. The active ingredient Trehalose, a disaccharide of glucose, is thought to induce autophagy and stimulate intracellular clearance of the protein aggregates. The drug is administered weekly by intravenous infusion.



Trehalose

- **Stem cell transplants**. Autologous stem cells are transplanted into the esophagus of the patient. Some short term efficacy but they still carry the genetic defect.

Pabparna™ is potentially a unique one-shot treatment for OPMD – simultaneously silencing the defective PABPN1 gene and replacing it with the wild type gene in the same cell.



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Dr Capucine Trollet
Pierre Klein
Gillian Butler-Browne

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