3 de julio de 2025

Del-01 ATG4B, a novel antisense oligonucleotide to treat ALS

Universitat de Lleida

Pascual Torres

Content

Content

Universitat de Lleida

Academia

48
Bachelor's degrees and double bachelor's degrees

10,674
Bachelor's degrees, master's degrees and PhD students

33
Master's degrees

2,024
Lifelong learning students

6,352
Extension programmes students

1,492
Professors and researchers

581
Administration and service staff

596,704
€ funding and grants for UdL programmes

1,118
Internship agreements

116.712
M€ budget

Academia

48
Bachelor's degrees and double bachelor's degrees

10,674
Bachelor's degrees, master's degrees and PhD students

33
Master's degrees

2,024
Lifelong learning students

6,352
Extension programmes students

1,492
Professors and researchers

581
Administration and service staff

596,704
€ funding and grants for UdL programmes

1,118
Internship agreements

116.712
M€ budget

Research

21.25
M€ resources for RDI

54
Research groups

706
Researchers

5
Research centres

19
Business Chairs

15
Doctorate programmes

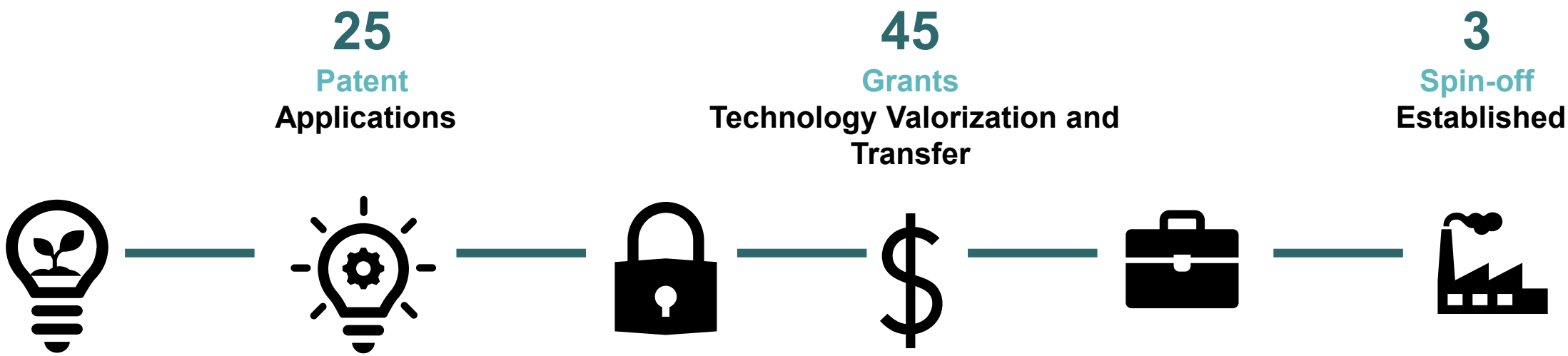
56%
Papers in first-quartile journals

35
Scientific and technical services

80'9%
Open access papers

31
Researchers among the most cited in the world

Innovation (2019-2023)



Innovation (2019-2023)

+ 80
Innovative Projects
Evaluated

25
Patent
Aplications

6
Granted
Patents

45
Grants
Technology Valorization and Transfer

7
Licensed
Technologies

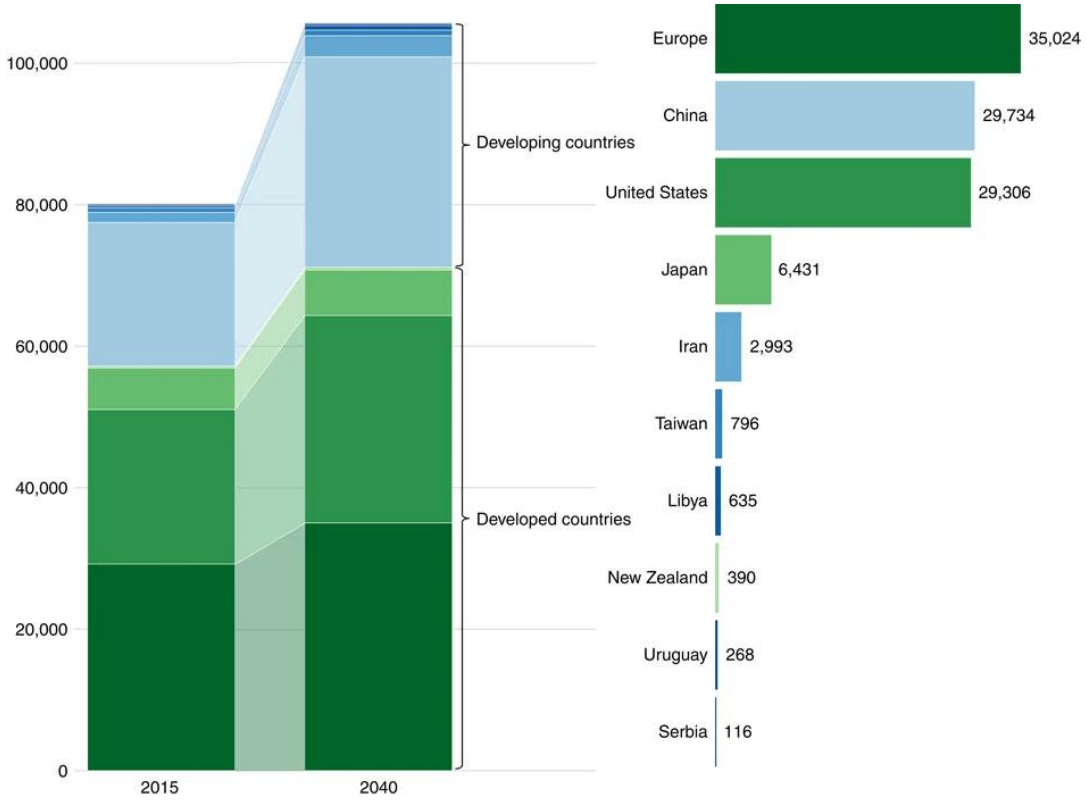
3
Spin-off
Established

+ 16 University–Industry Chairs

Content

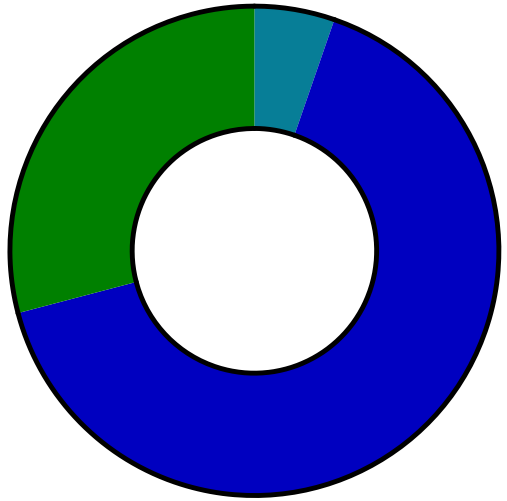
Amyotrophic Lateral Sclerosis (ALS)

ALS prevalence



Arthur et al., 2016

Annual Cost/Patient (€)

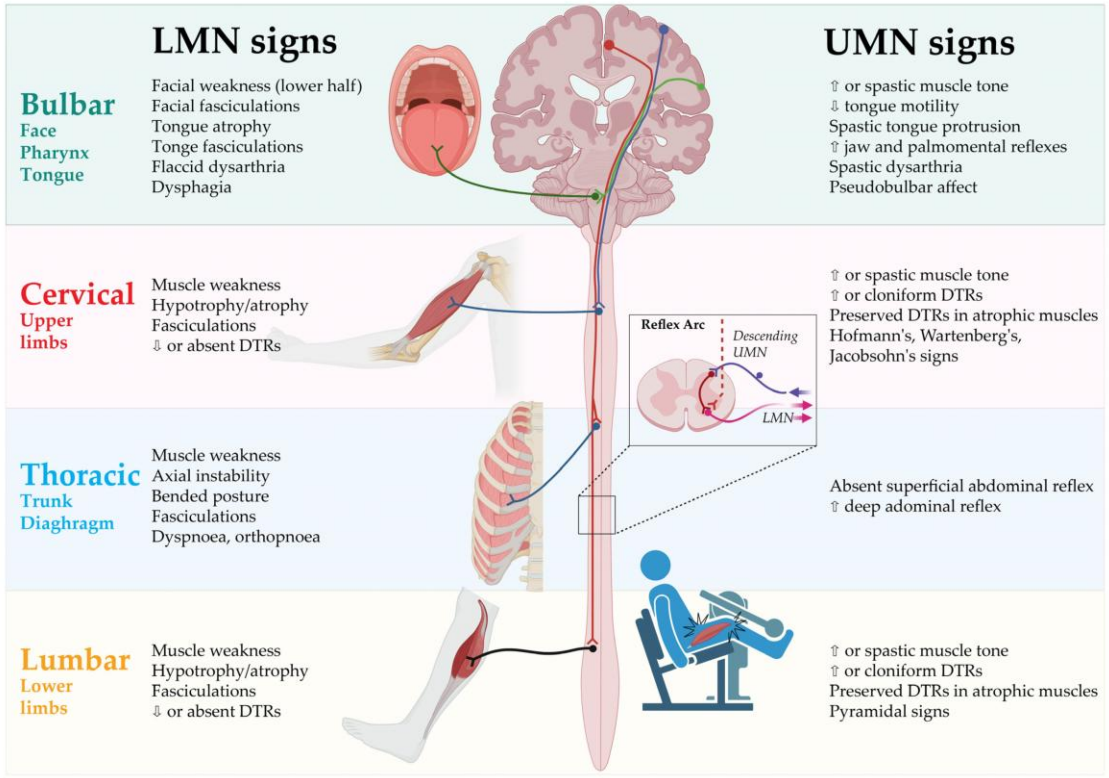


5.31% Medical
65.59% Non-medical
29.10% Indirect

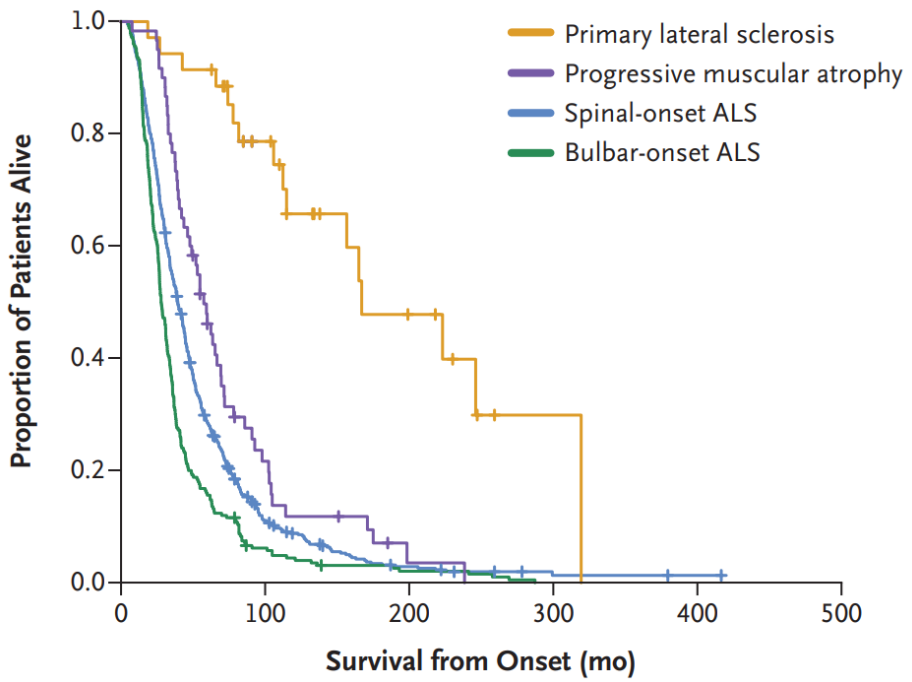
Total = 43,823 €

López-Bastida et al., 2009

Amyotrophic Lateral Sclerosis (ALS)

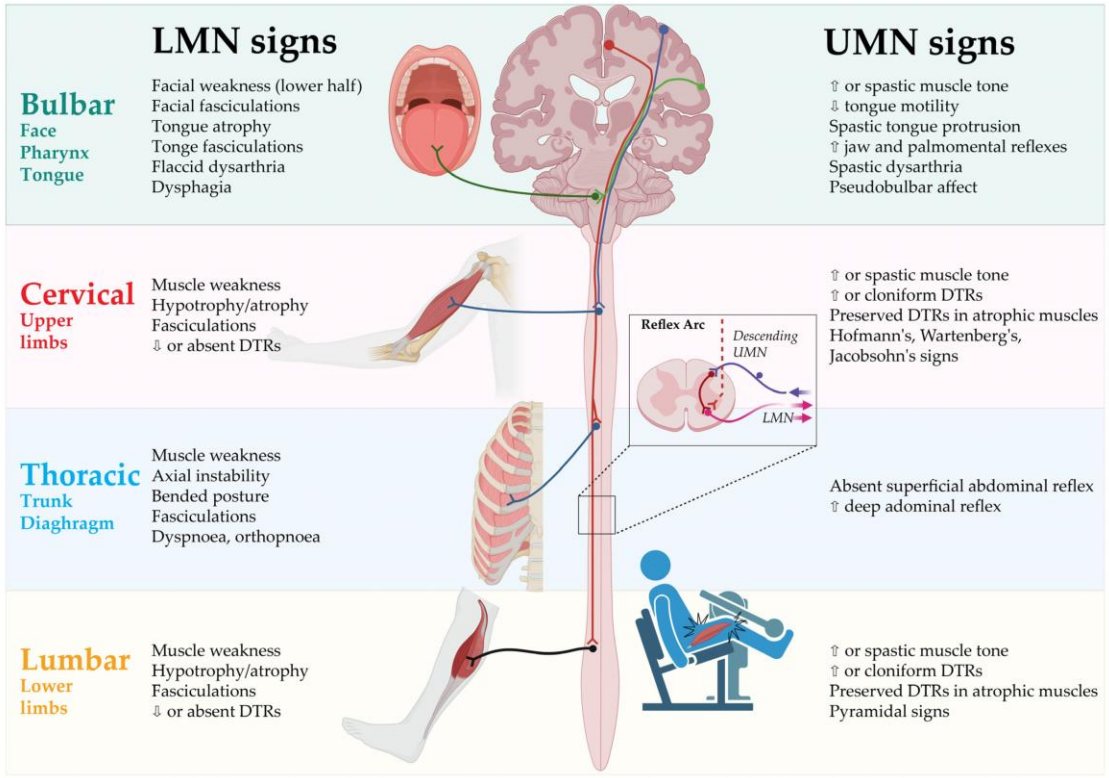


Vidovic et al., 2023

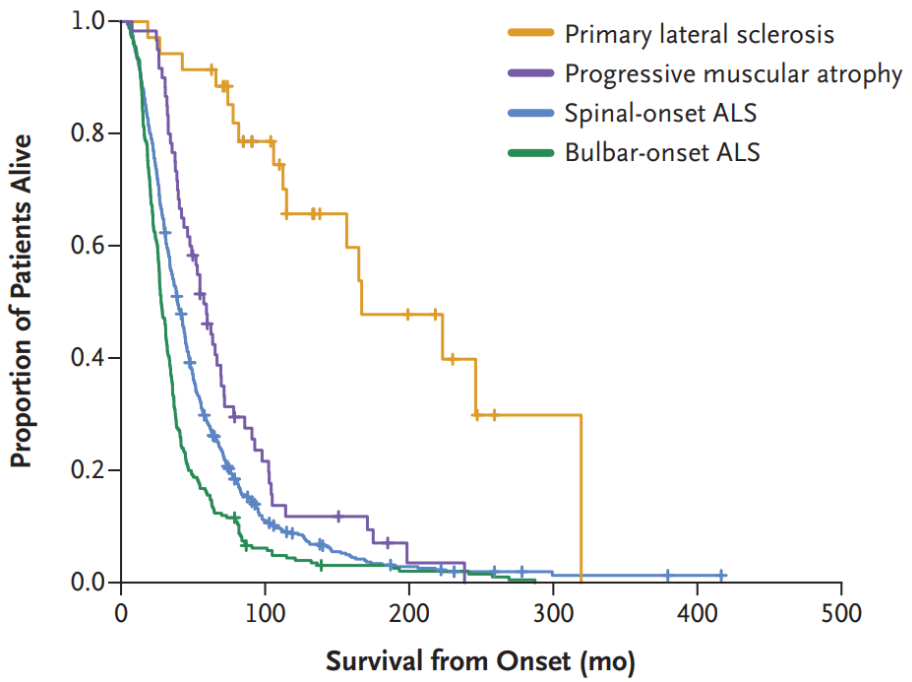


Brown et al., 2017

Amyotrophic Lateral Sclerosis (ALS)



Vidovic et al., 2023



Brown et al., 2017

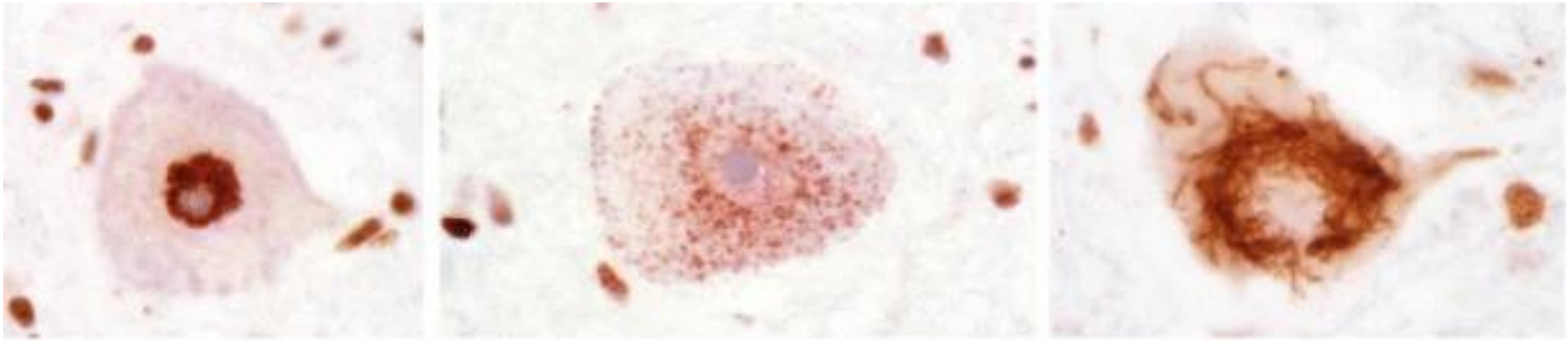
Lifetime risk 1:400

Content

TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



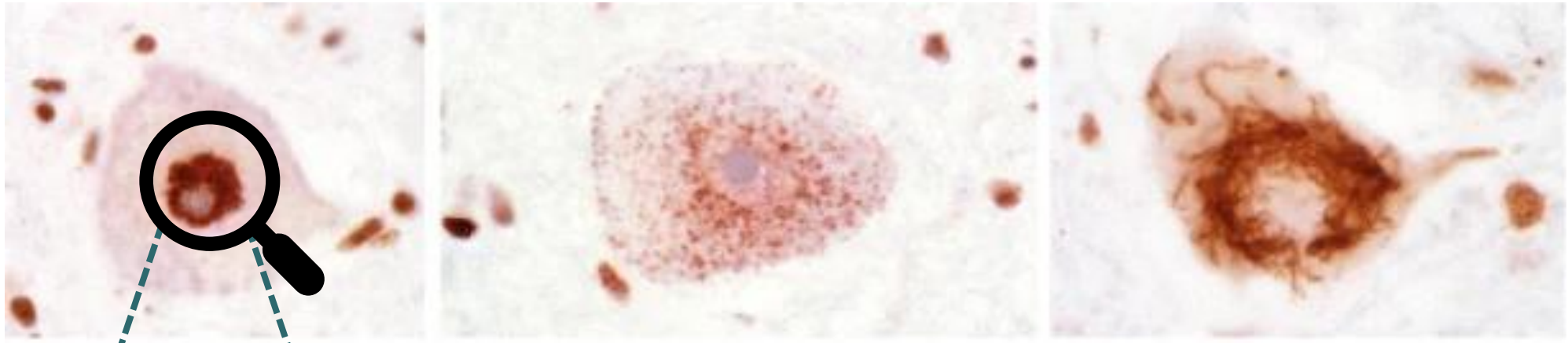
Feneberg et al., 2018

Nucleus → **Cytoplasm**

TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



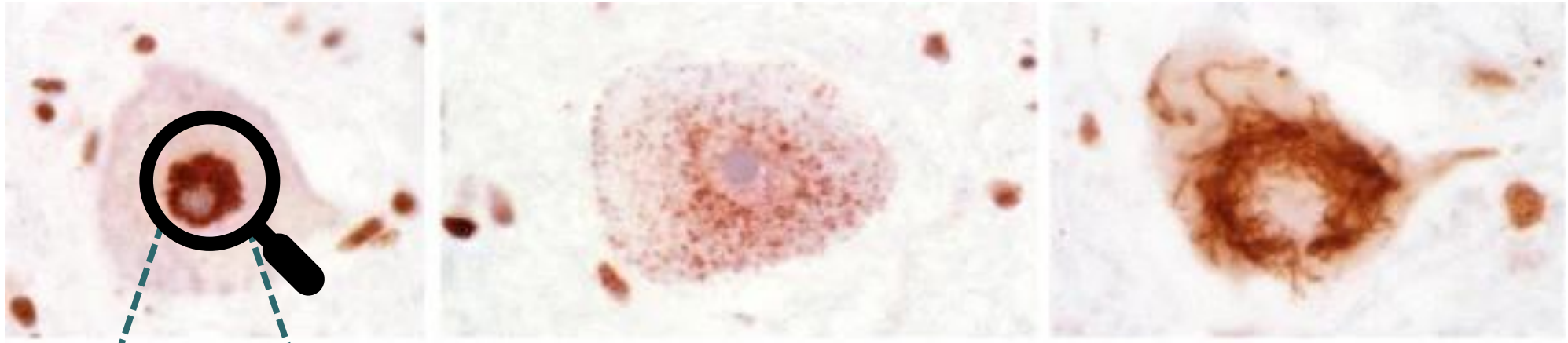
Feneberg et al., 2018

ATG4B pre-mRNA

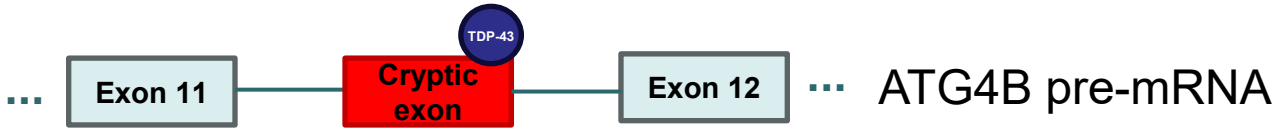
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



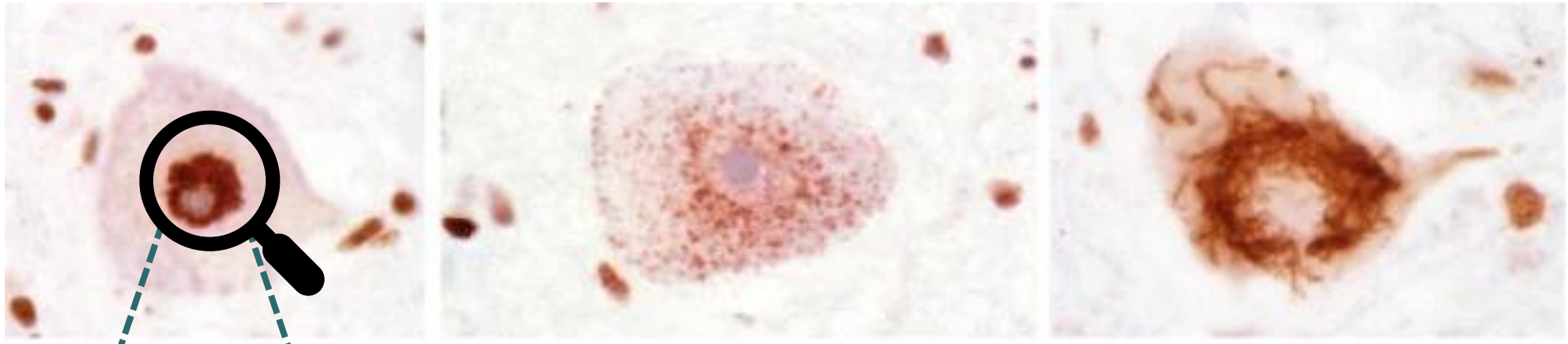
Feneberg et al., 2018



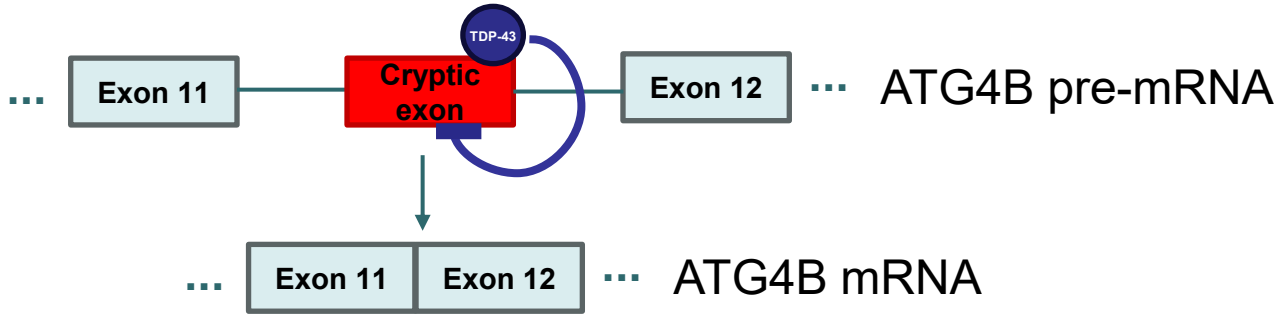
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



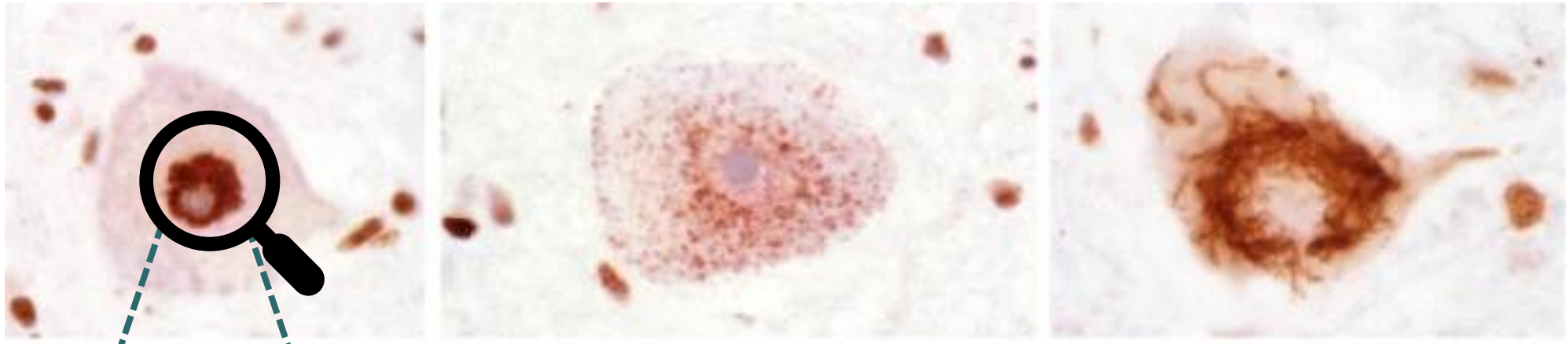
Feneberg et al., 2018



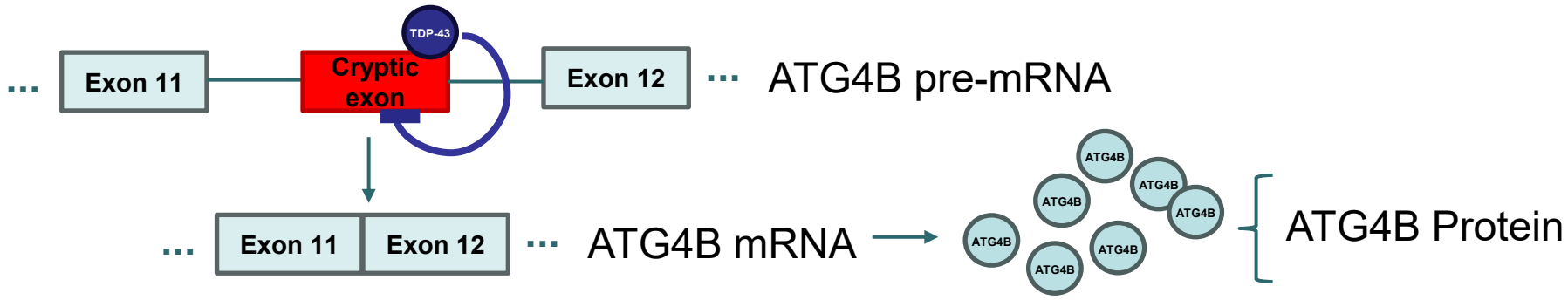
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



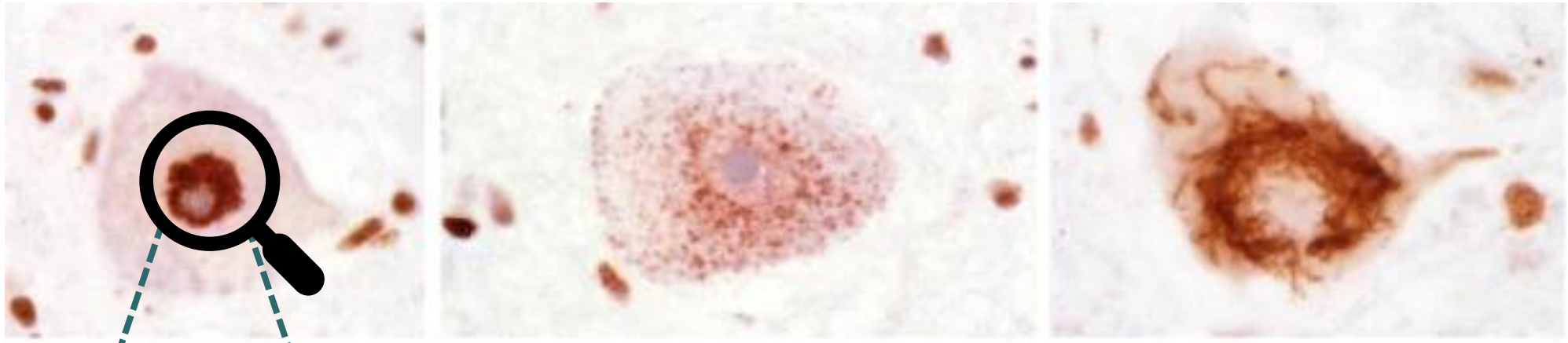
Feneberg et al., 2018



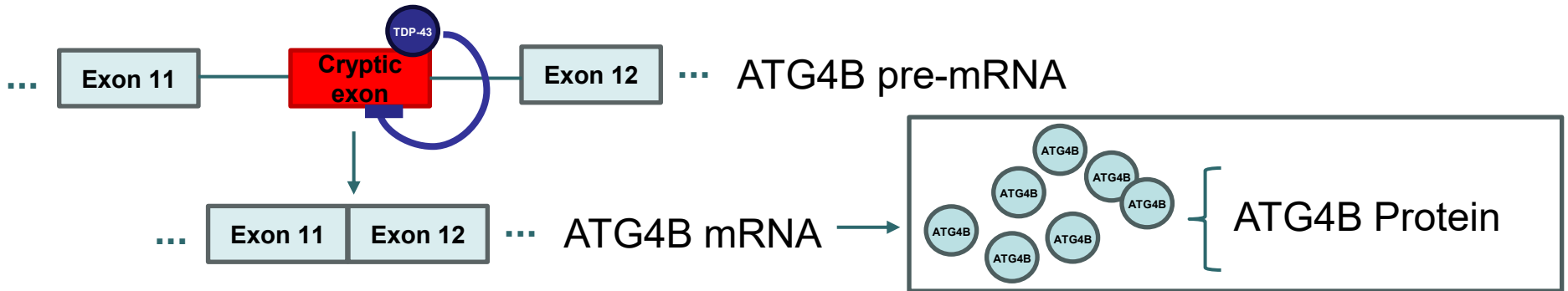
TDP-43 mislocalization in Motor Neurons

Healthy Control

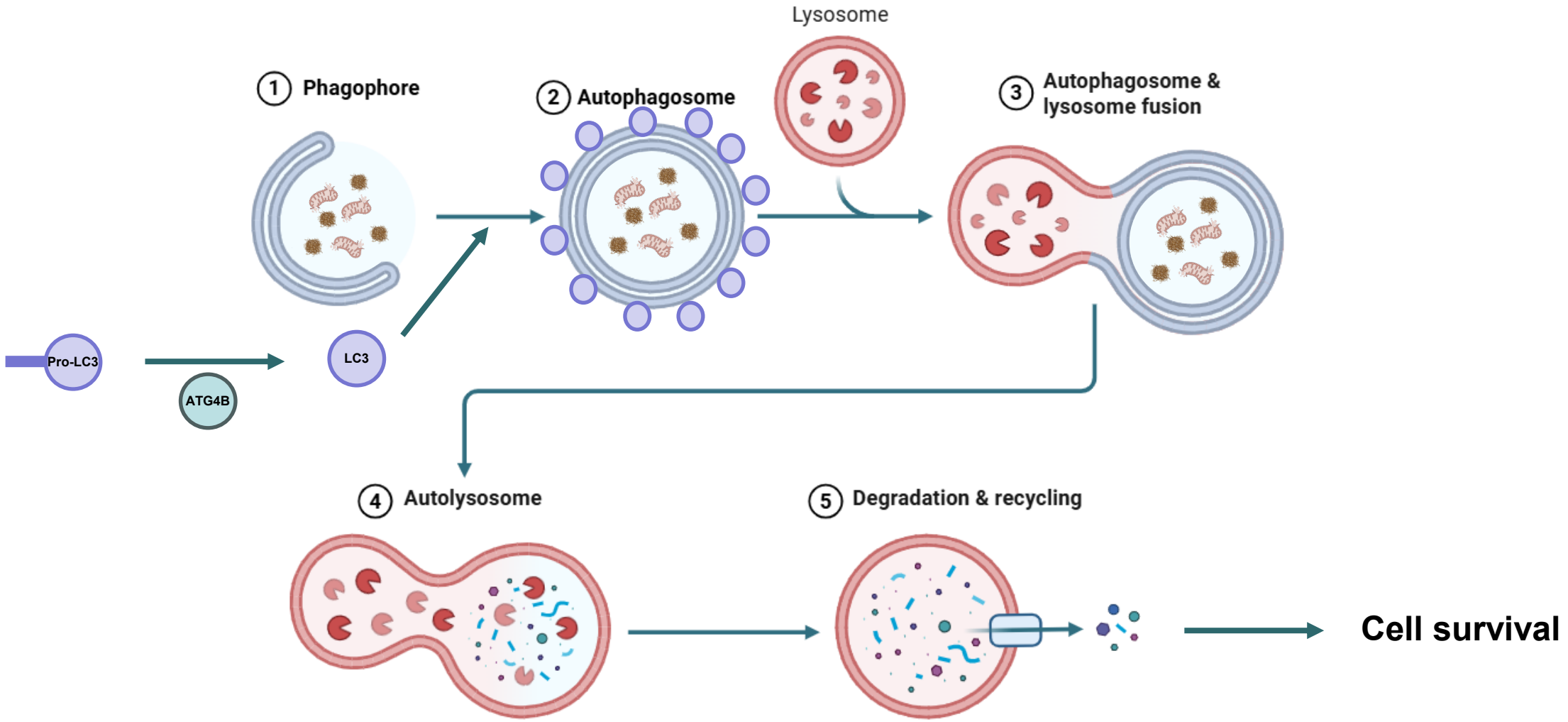
ALS



Feneberg et al., 2018



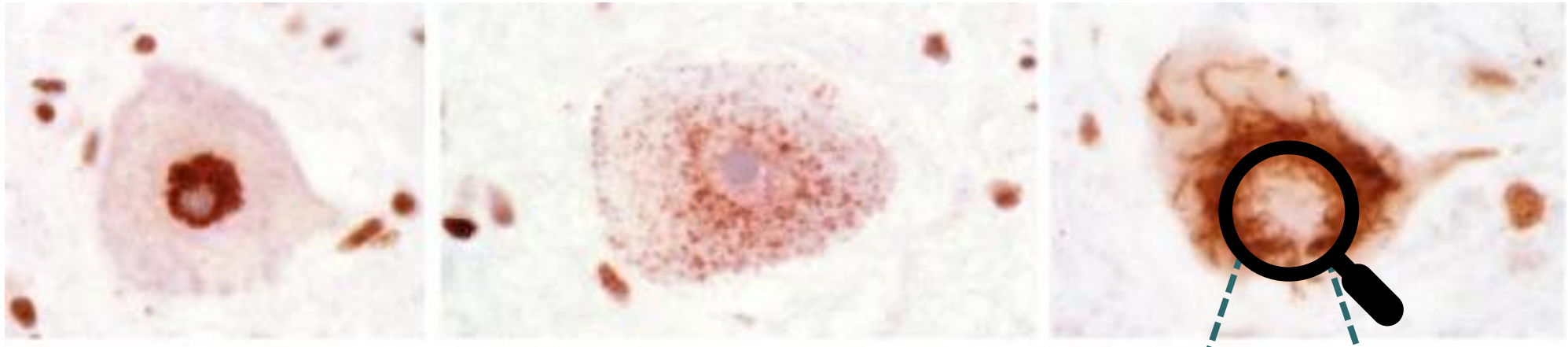
ATG4B function



TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS

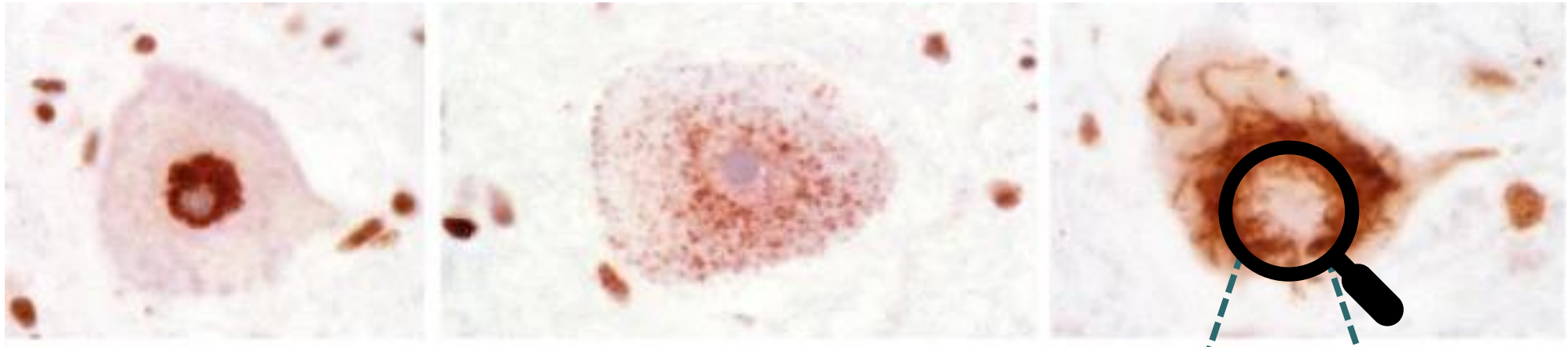


Feneberg et al., 2018

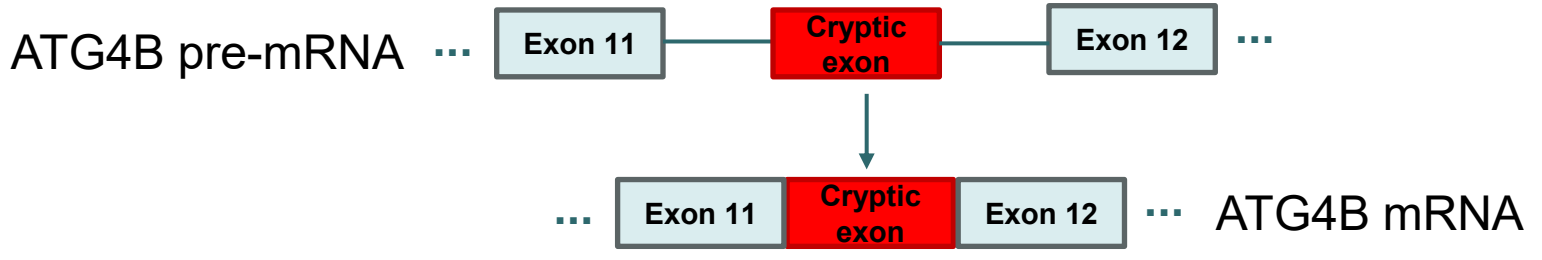
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



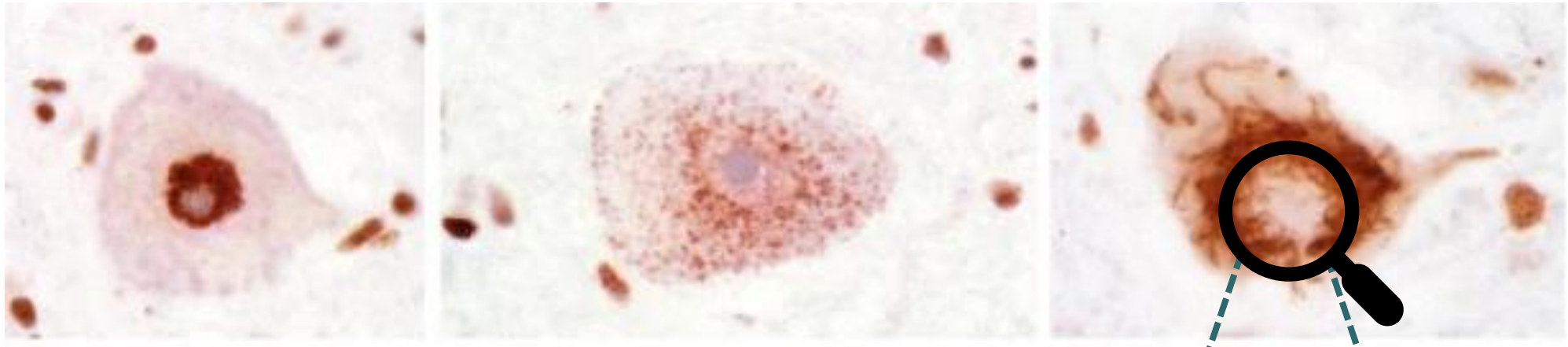
Feneberg et al., 2018



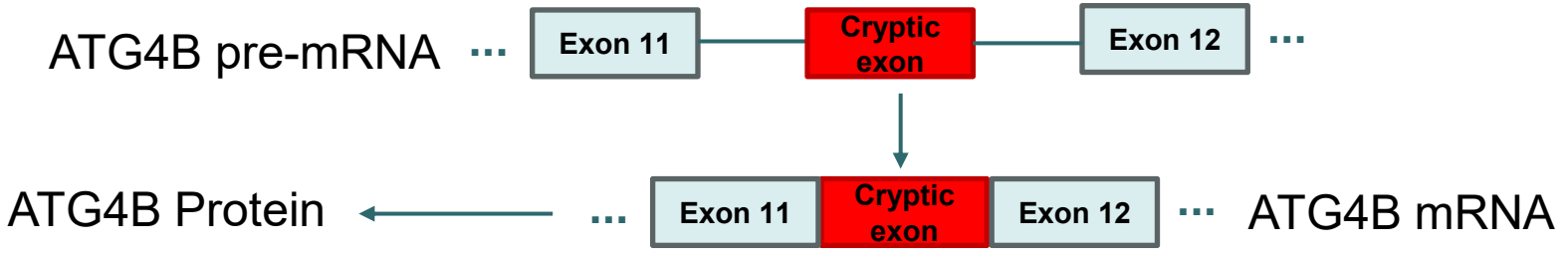
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



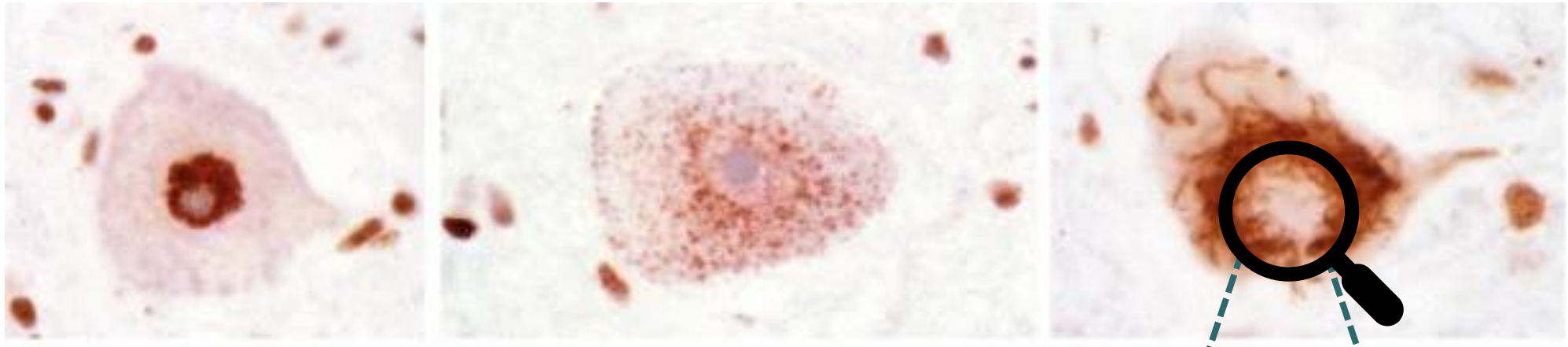
Feneberg et al., 2018



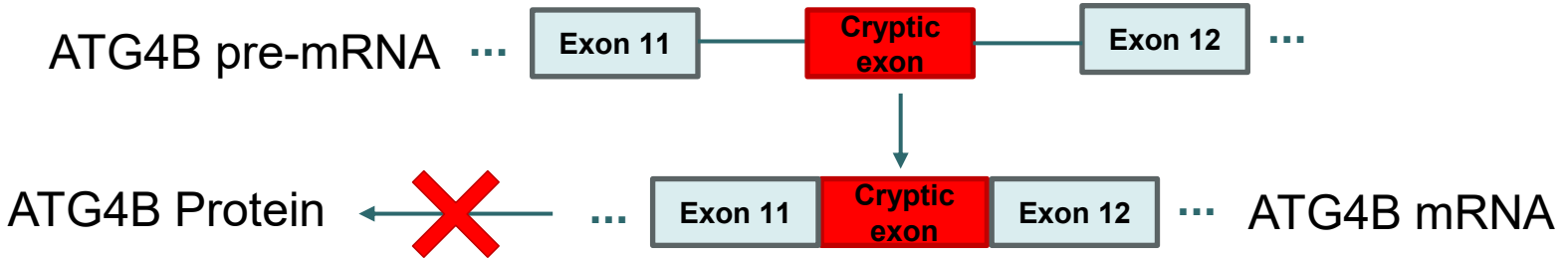
TDP-43 mislocalization in Motor Neurons

Healthy Control

ALS



Feneberg et al., 2018

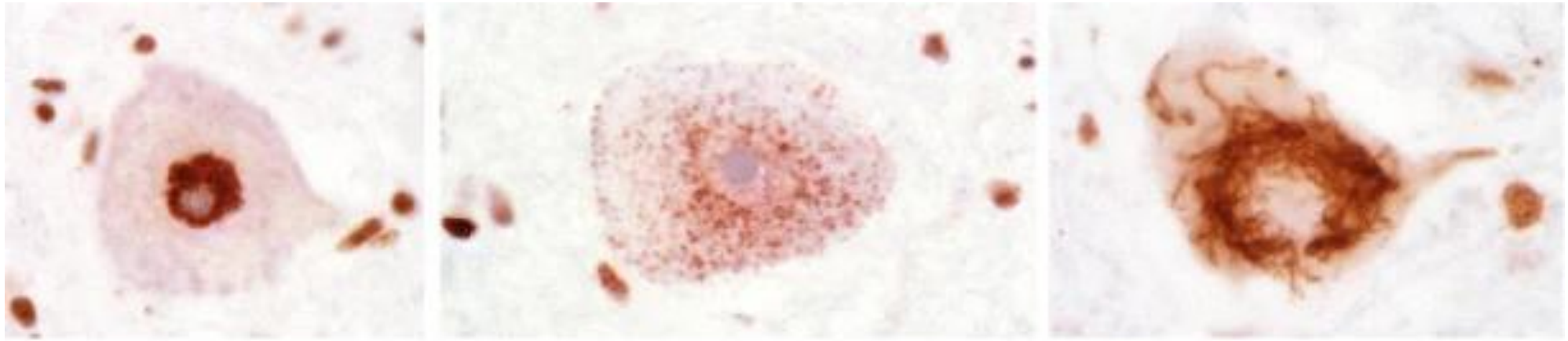


TDP-43 mislocalization in Motor Neurons

Healthy Control

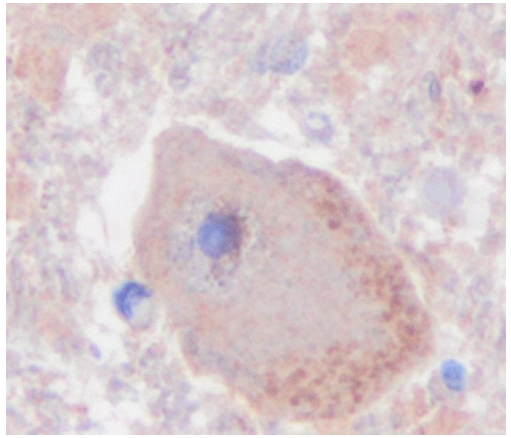
ALS

TDP-43

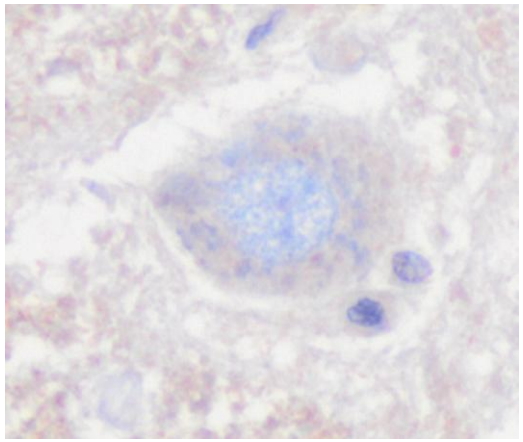


Feneberg et al., 2018

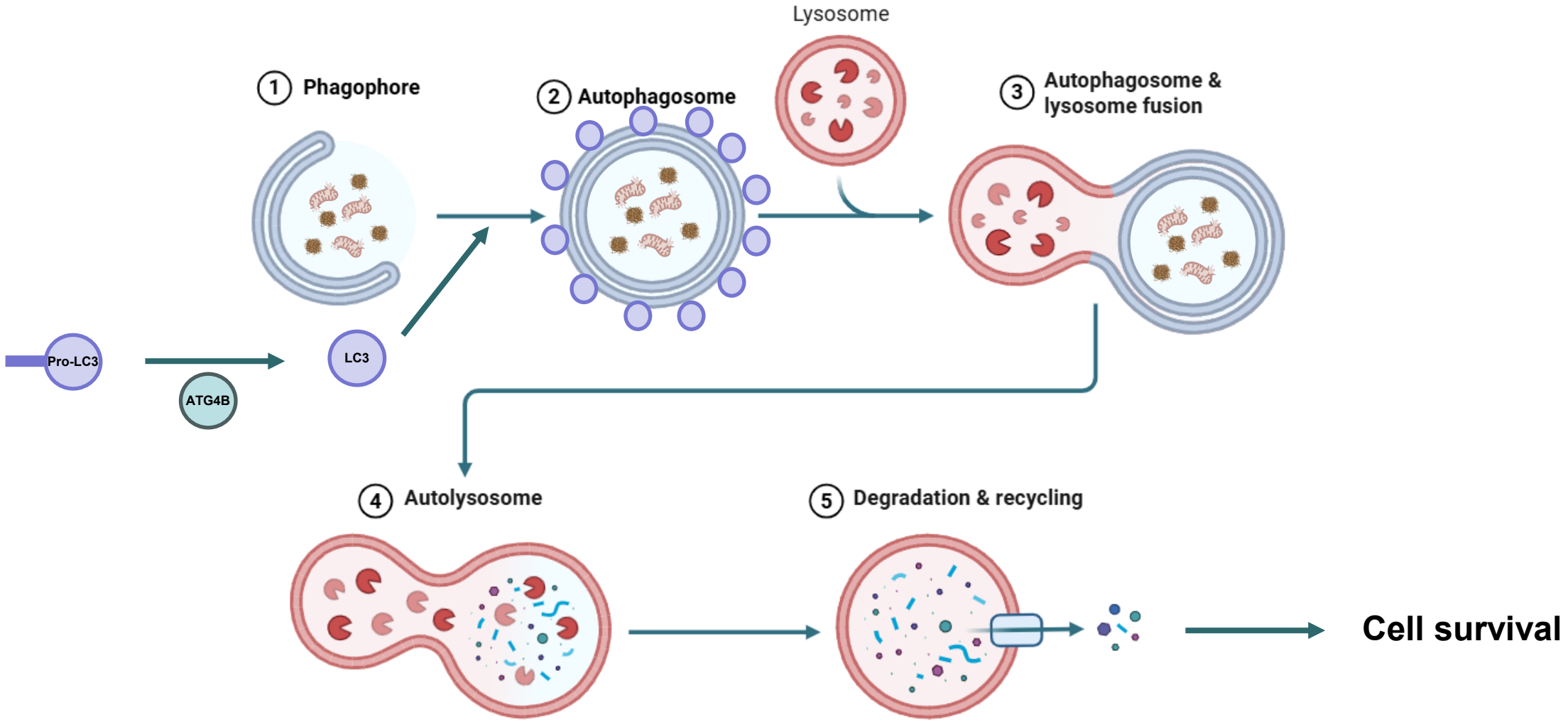
ATG4B



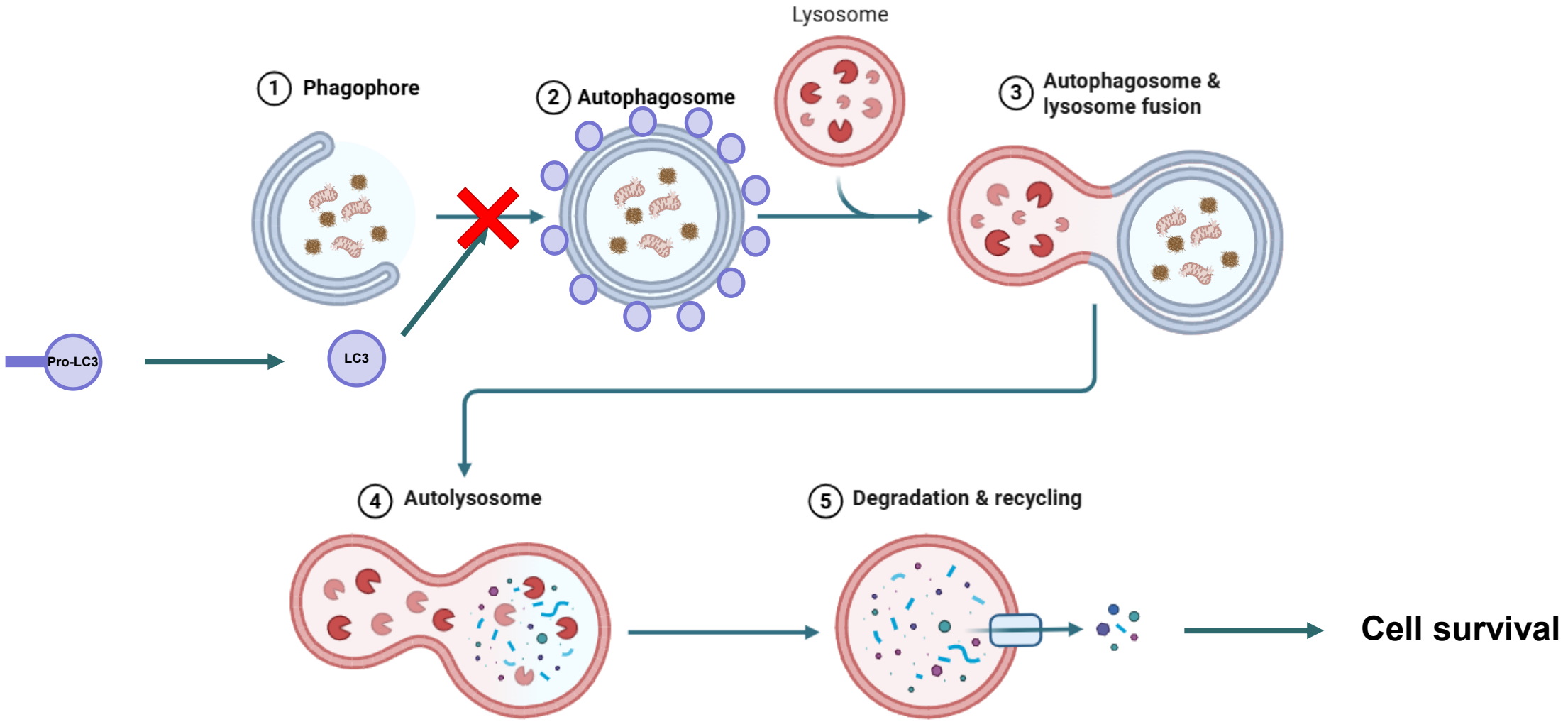
Loss of ATG4B expression



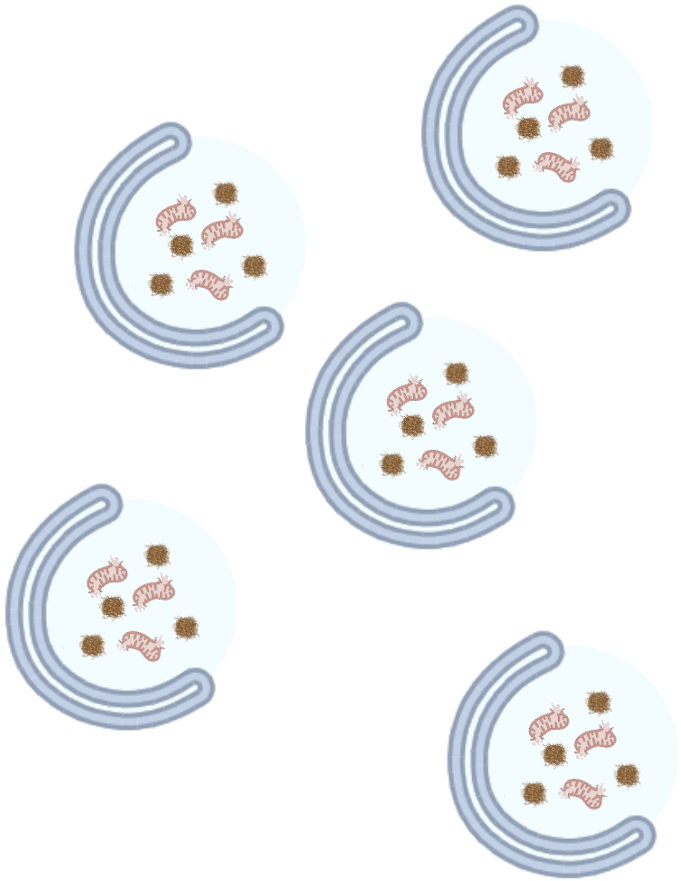
ATG4B loss of function



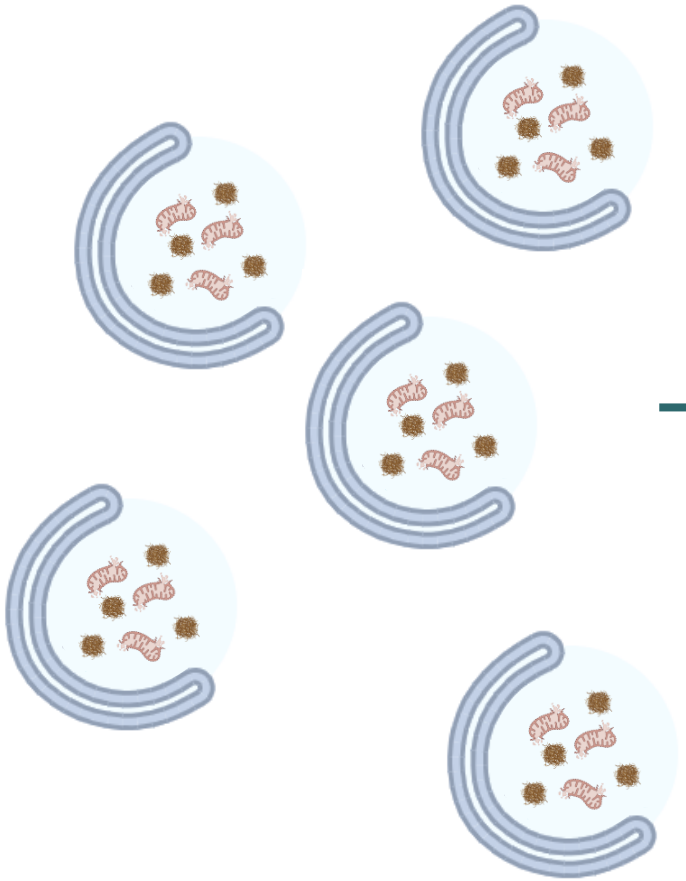
ATG4B loss of function



ATG4B loss of function

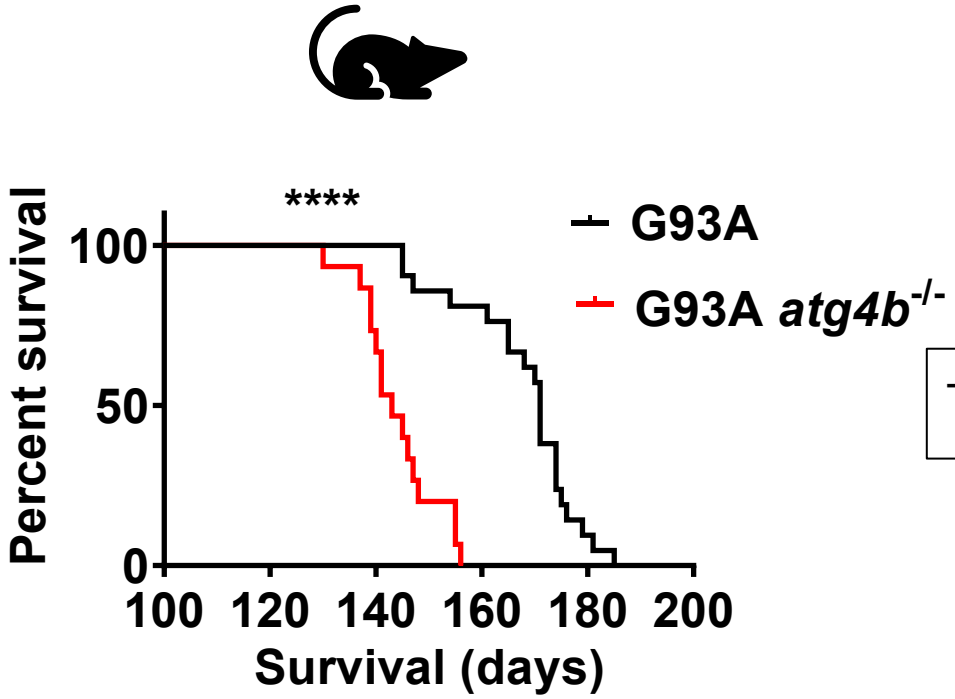


ATG4B loss of function



- Dysfunctional mitochondria accumulation.
- Protein aggregation.
- Cell stress.
- Neurodegeneration.

ATG4B loss of function

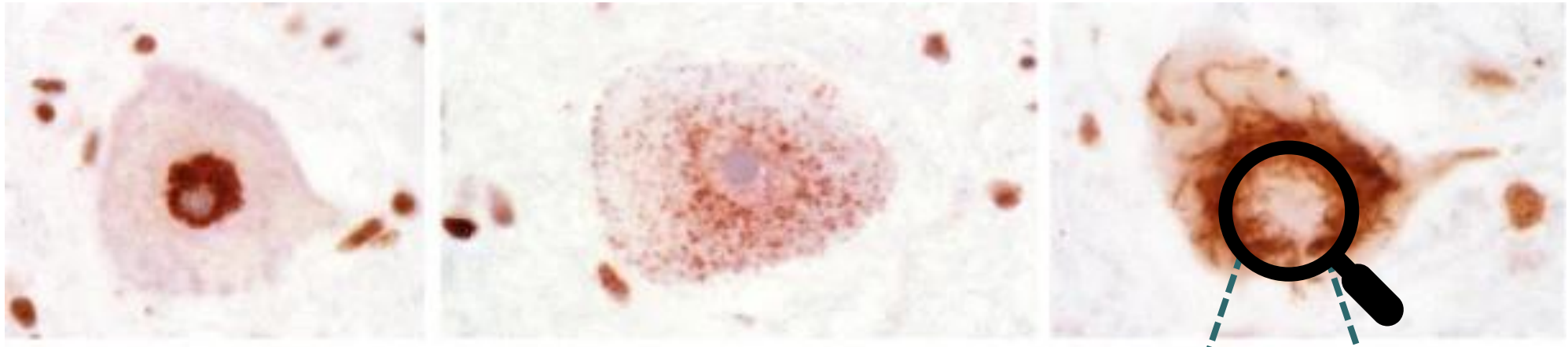


- The deletion of Atg4b in ALS mouse model shortens the survival time more than 60%

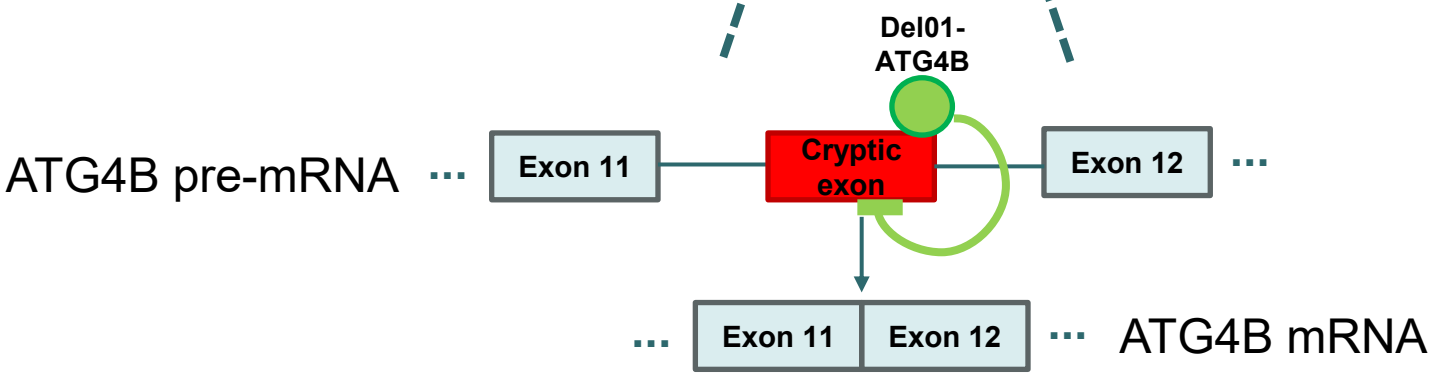
Del01-ATG4B mechanism of action

Healthy Control

ALS



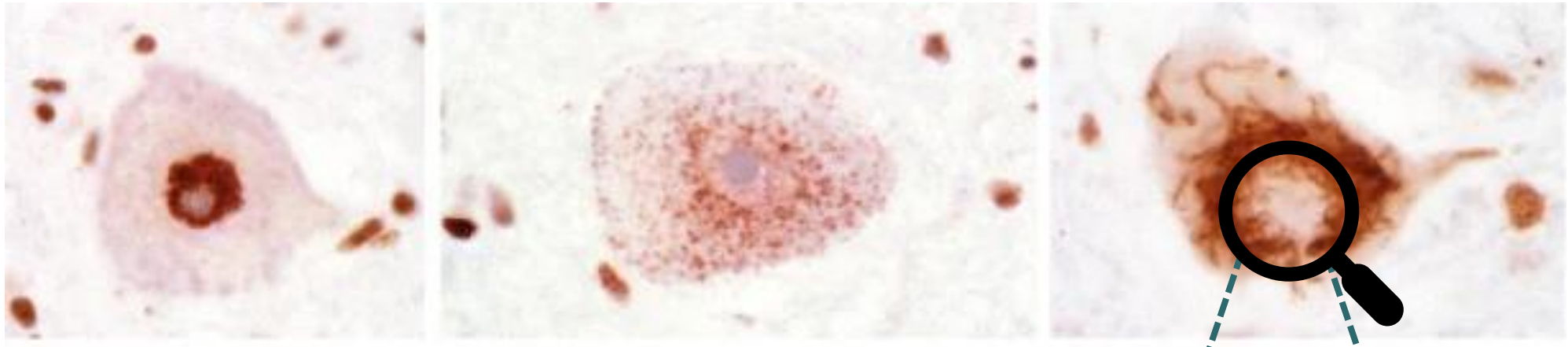
Feneberg et al., 2018



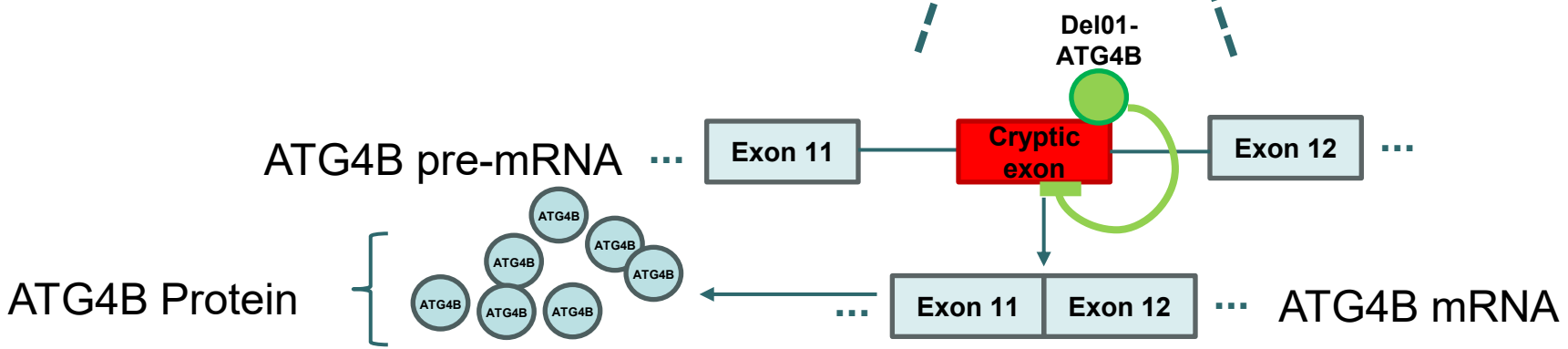
Del01-ATG4B mechanism of action

Healthy Control

ALS



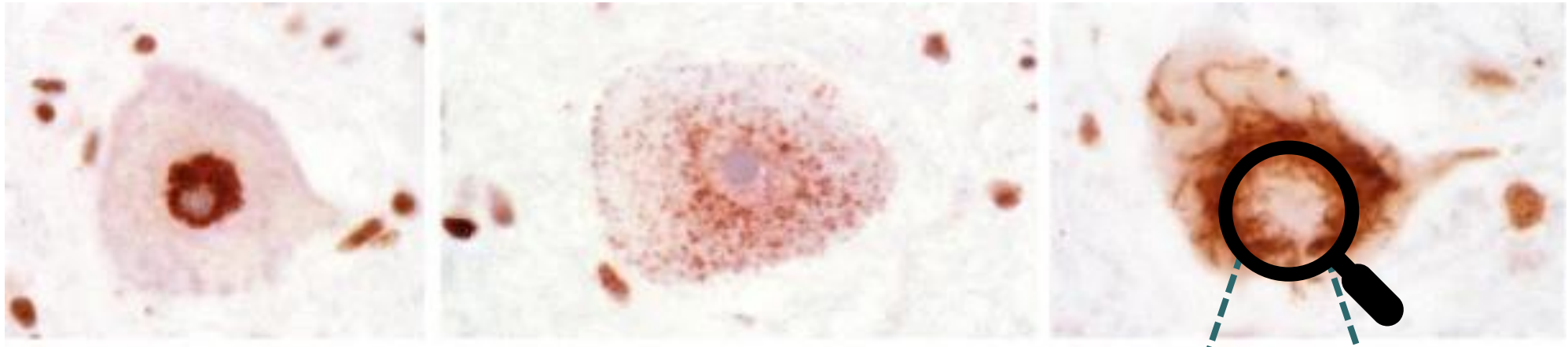
Feneberg et al., 2018



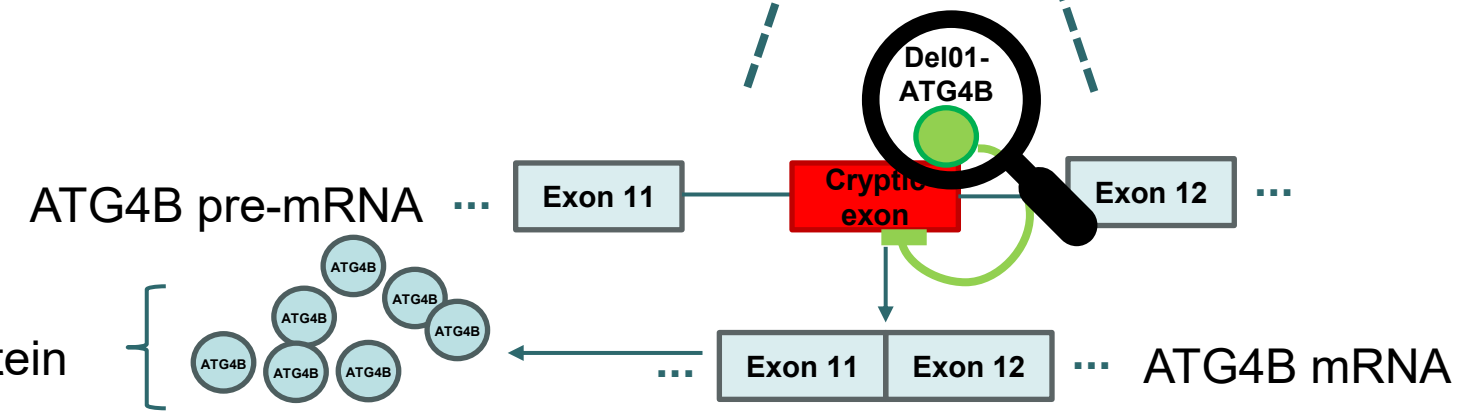
Del01-ATG4B mechanism of action

Healthy Control

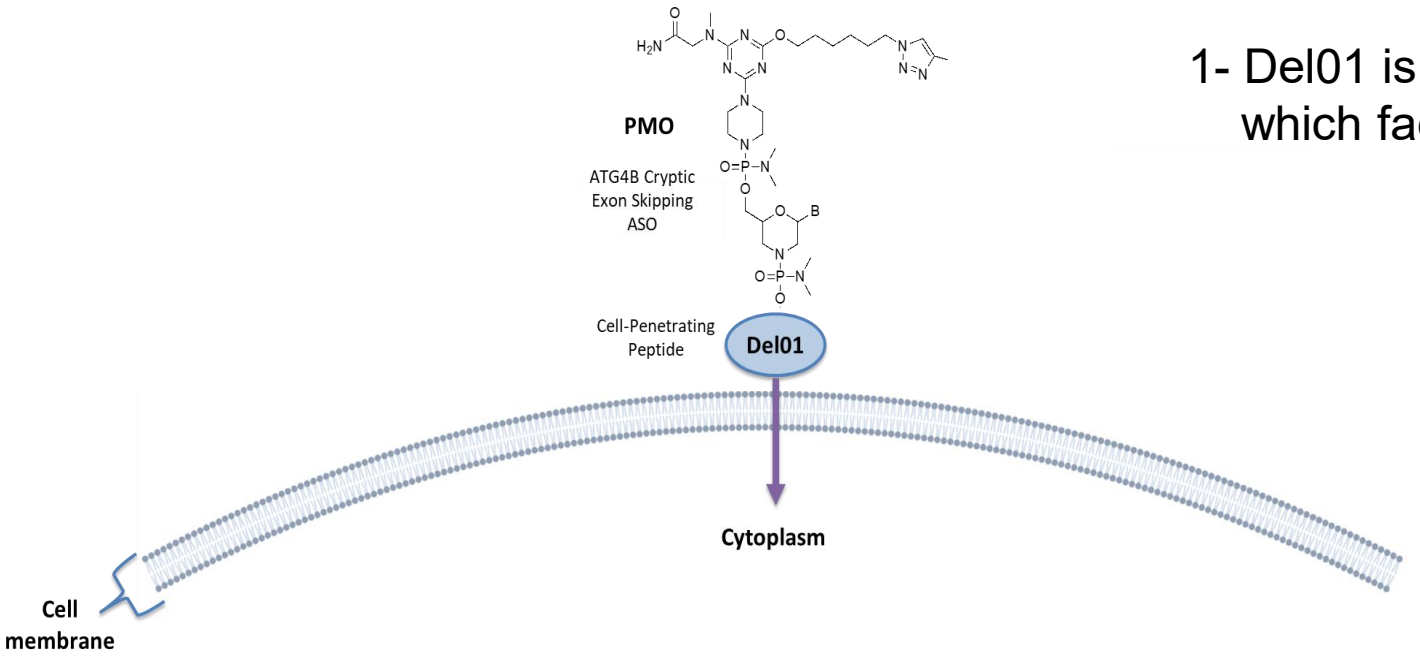
ALS



Feneberg et al., 2018

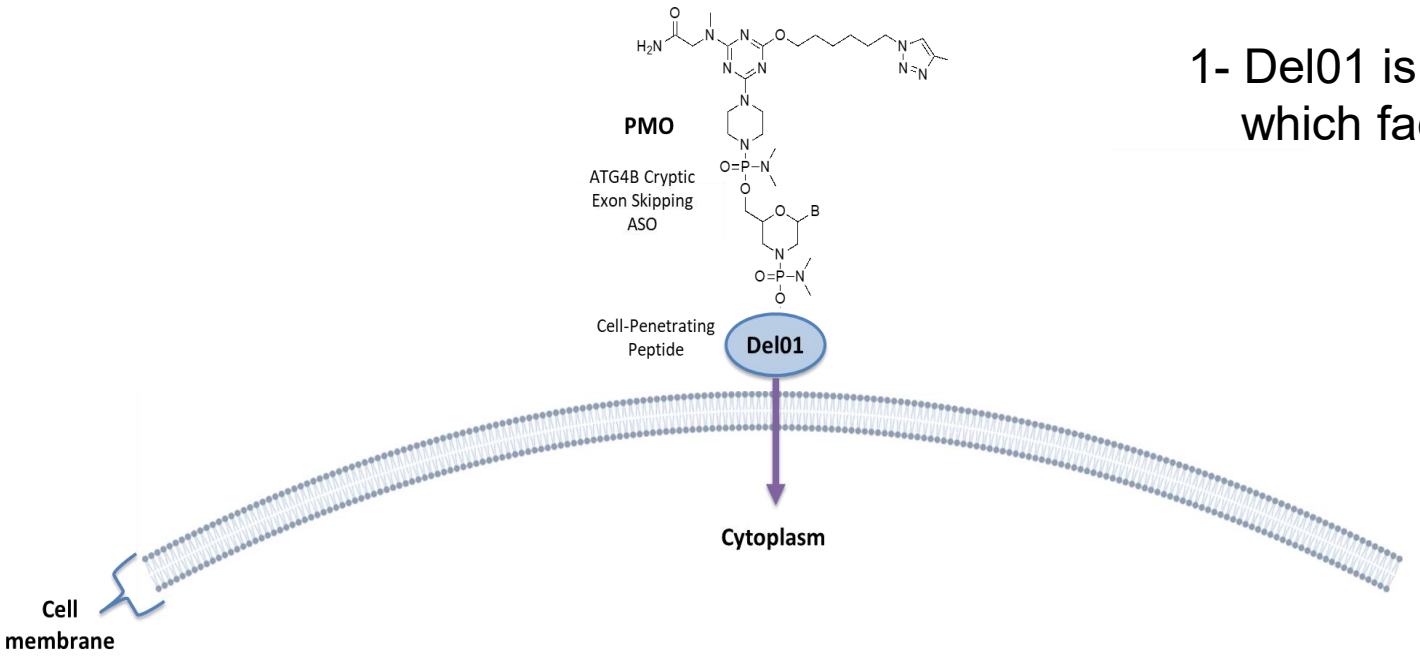


Del01-ATG4B mechanism of action

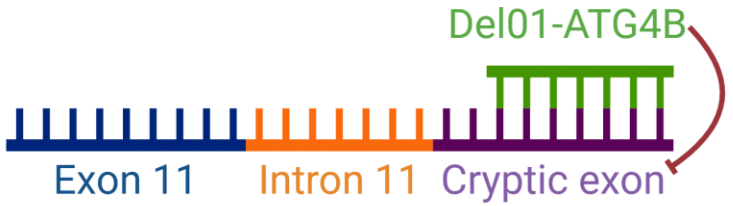


1- Del01 is a cell penetrating peptide which facilitates cellular intake.

Del01-ATG4B mechanism of action

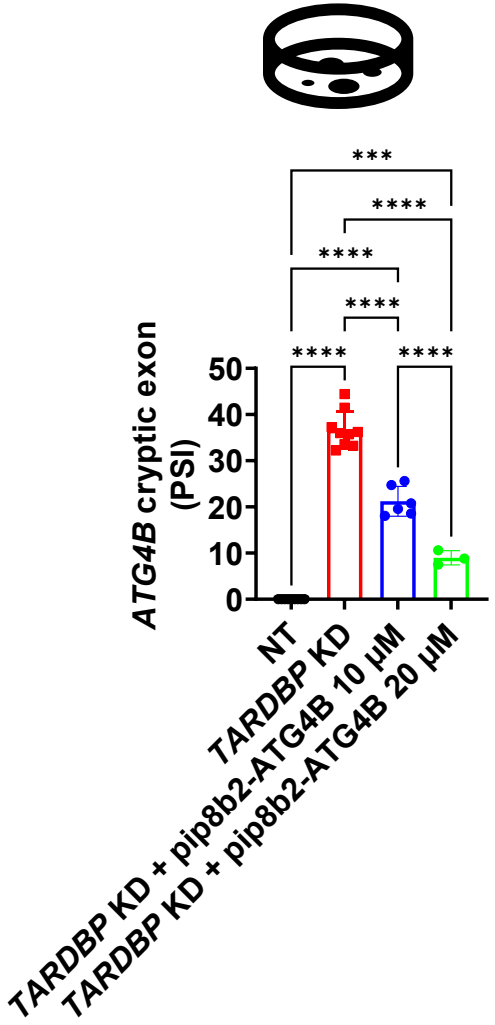


1- Del01 is a cell penetrating peptide which facilitates cellular intake.



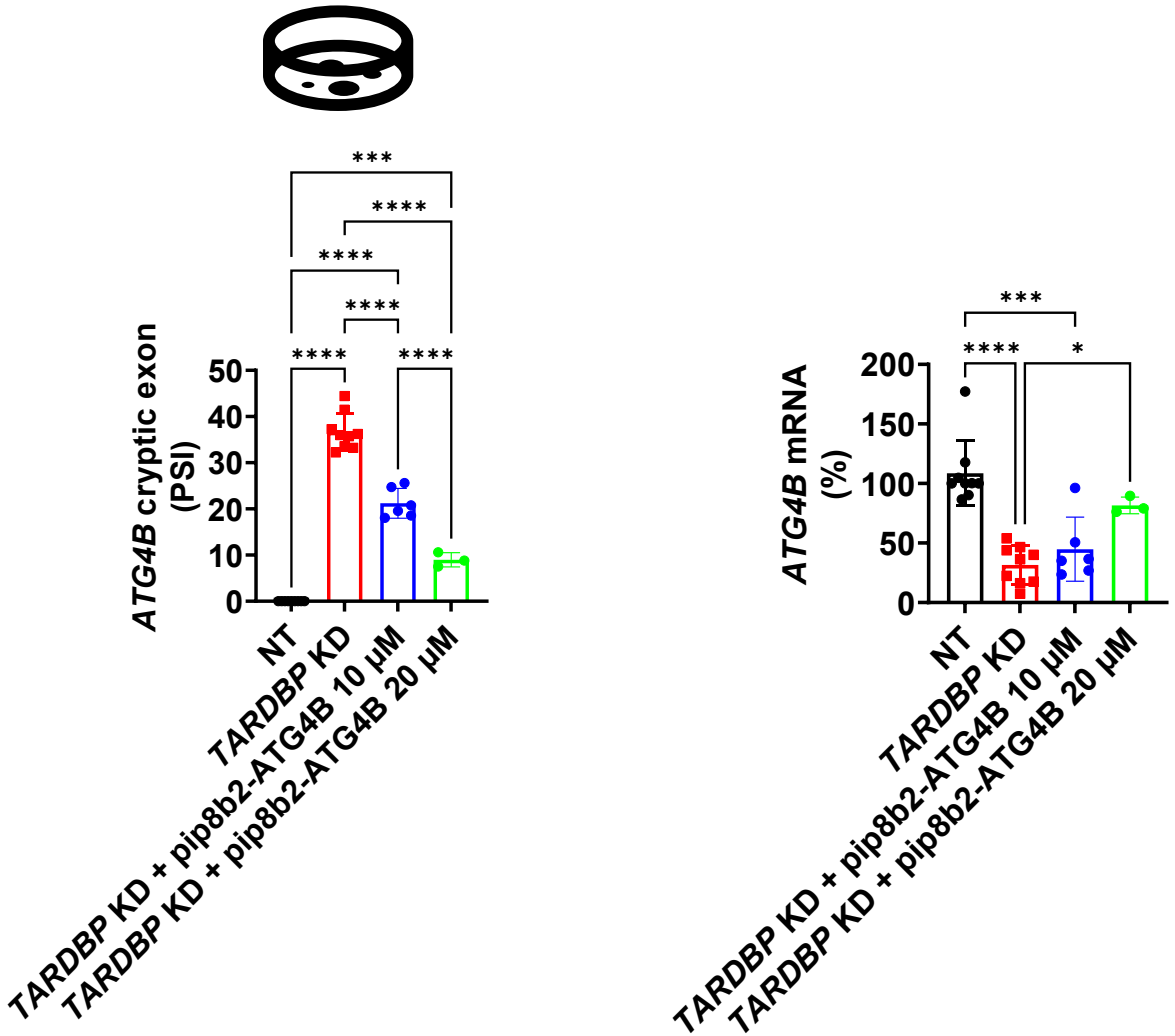
2- ATG4B PMO sequence is an antisense oligonucleotide (**ASO**) which prevents cryptic exon splicing.

Del01-ATG4B mechanism of action



1- PMO sequence of Del01-ATG4B prevents cryptic exon splicing in cells.

Del01-ATG4B mechanism of action



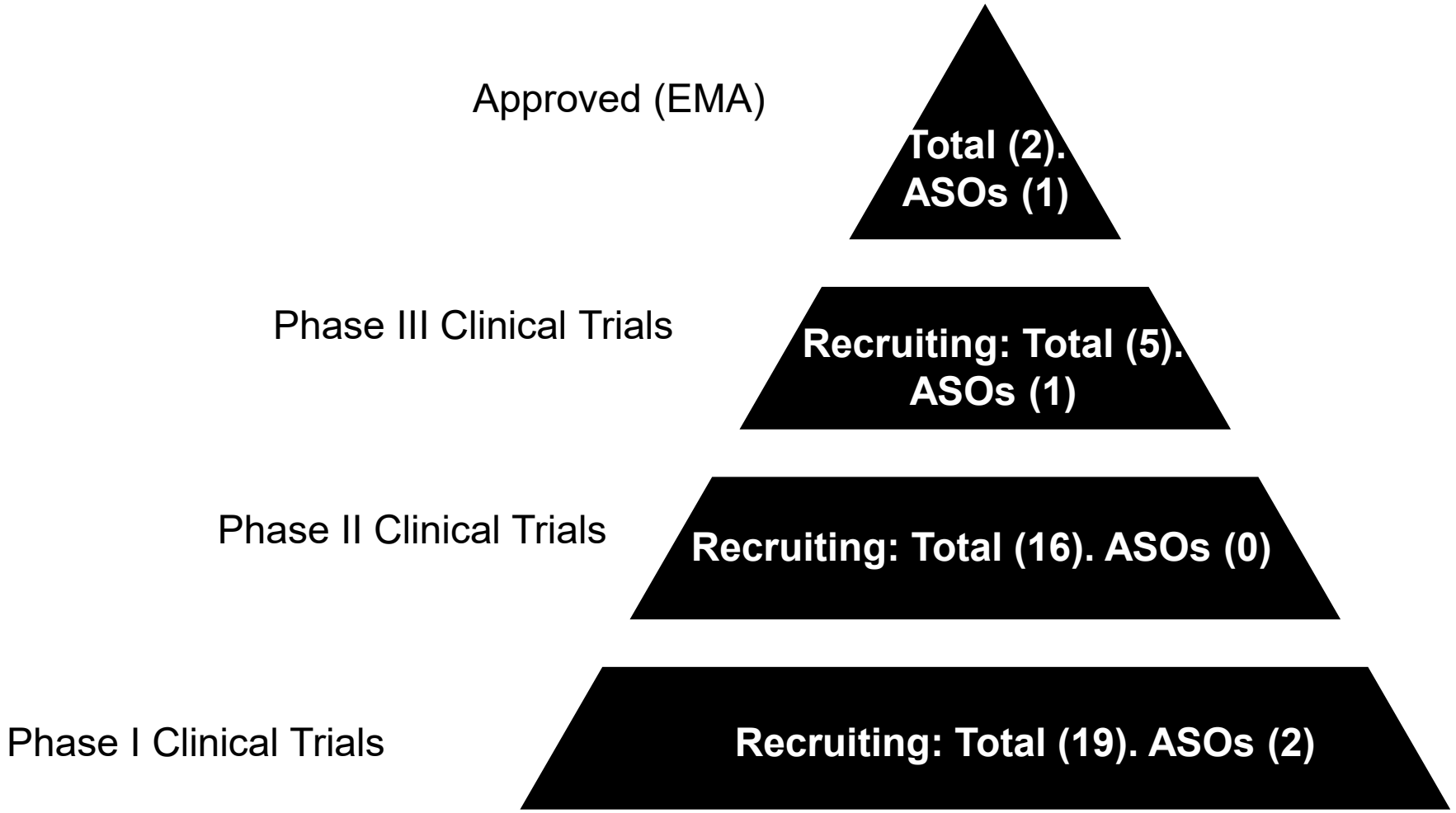
1- PMO sequence of Del01-ATG4B prevents cryptic exon splicing in cells.

2- PMO sequence of Del01-ATG4B restores normal mRNA levels in cells

Content

Competitive landscape

Competitive landscape



Main competitors

1. **QRL-201 (Phase I):** An ASO which targets STMN2 cryptic exon. Promotes neurite growth. Different mechanism of action. Potentially complementary. Eligibility: 97 % of ALS patients.

Main competitors

1. **QRL-201 (Phase I):** An ASO which targets STMN2 cryptic exon. Promotes neurite growth. Different mechanism of action. Potentially complementary. Eligibility: 97 % of ALS patients.

2. **ION363 (Phase III):** An ASO which targets FUS. Downregulate mutant FUS mRNA with a clear clinical benefit. **Eligibility: < 1 % of ALS patients.**

Main competitors

1. **QRL-201 (Phase I):** An ASO which targets STMN2 cryptic exon. Promotes neurite growth. Different mechanism of action. Potentially complementary. Eligibility: 97 % of ALS patients.

2. **ION363 (Phase III):** An ASO which targets FUS. Downregulate mutant FUS mRNA with a clear clinical benefit. **Eligibility: < 1 % of ALS patients.**

3. **Tofersen (EMA/FDA approved):** An ASO which targets SOD1. Downregulate SOD1 mRNA with a clear clinical benefit in some patients. **Eligibility: < 2 % of ALS patients.**

Main competitors

1. **QRL-201 (Phase I):** An ASO which targets STMN2 cryptic exon. Promotes neurite growth. Different mechanism of action. Potentially complementary. Eligibility: 97 % of ALS patients.

2. **ION363 (Phase III):** An ASO which targets FUS. Downregulate mutant FUS mRNA with a clear clinical benefit. **Eligibility: < 1 % of ALS patients.**

3. **Tofersen (EMA/FDA approved):** An ASO which targets SOD1. Downregulate SOD1 mRNA with a clear clinical benefit in some patients. **Eligibility: < 2 % of ALS patients.**

4. **Riluzole (EMA/FDA approved):** An antiglutamatergic drug **with a short survival benefit of 2–3 months.** Eligibility: 100 % of ALS patients.

Content

Milestones

1. **In vitro efficacy:** PMO sequence of Del01-ATG4B prevents ATG4B cryptic exon splicing and restores normal mRNA levels.

Milestones

1. **In vitro efficacy:** PMO sequence of Del01-ATG4B prevents ATG4B cryptic exon splicing and restores normal mRNA levels.

Milestones

1. **In vitro efficacy:** PMO sequence of Del01-ATG4B prevents ATG4B cryptic exon splicing and restores normal mRNA levels.

2. **Del01-ATG4B is safe:** Acute intracisternal administration in mice reports low toxicity and any evidence of neuropathological finding.

Milestones

1. **In vitro efficacy:** PMO sequence of Del01-ATG4B prevents ATG4B cryptic exon splicing and restores normal mRNA levels.

2. **Del01-ATG4B is safe:** Acute intracisternal administration in mice reports low toxicity and any evidence of neuropathological finding.

3. **Del01-ATG4B targets motor neurons:** Motor neurons (the main affected cells in ALS) internalize Del01-ATG4B and persists in tissue for more than 1 week.

Milestones

1. **In vitro efficacy:** PMO sequence of Del01-ATG4B prevents ATG4B cryptic exon splicing and restores normal mRNA levels.

2. **Del01-ATG4B is safe:** Acute intracisternal administration in mice reports low toxicity and any evidence of neuropathological finding.

3. **Del01-ATG4B targets motor neurons:** Motor neurons (the main affected cells in ALS) internalize Del01-ATG4B and persists in tissue for more than 1 week.

4. **A regulatory roadmap and an AEMPS classification for Del01-ATG4B are completed.**

Content

IPR protection

Both the ASO sequence (ATG4B PMO) and the CPP (Del01) –the main components of Del01-ATG4B- are patent protected (**PCT/EP2024/079389**), including relevant variants that could be used for the same therapeutic purpose or that may compete with our approach. International Filing Date 17.10.2024.

Content

Risk	Contingency plan
1. Low efficacy *in vivo*	

Risk	Contingency plan
1. Low efficacy *in vivo*	1. Test another protected sequence

Risk	Contingency plan
1. Low efficacy *in vivo*	1. Test another protected sequence
2. Toxicity over therapeutic dose	

Risk	Contingency plan
1. Low efficacy *in vivo*	1. Test another protected sequence
2. Toxicity over therapeutic dose	2. Test another CPP

Risk	Contingency plan
1. Low efficacy *in vivo*	1. Test another protected sequence
2. Toxicity over therapeutic dose	2. Test another CPP
3. Delayed funding or prolonged negotiation with external partners	

Risk	Contingency plan
1. Low efficacy *in vivo*	1. Test another protected sequence
2. Toxicity over therapeutic dose	2. Test another CPP
3. Delayed funding or prolonged negotiation with external partners	3. Consider launching a spin-off to accelerate development

Content

Partnering Opportunities

- **Licensing Agreement**

Open to discuss exclusive or non-exclusive rights depending on territory and indication

- **Co-development Partnership**

Shared development responsibilities and milestones
Opportunity to contribute expertise and funding in exchange for future returns

- **Option-to-License Agreement**

Partner provides funding for specific preclinical milestones (e.g., in vivo studies)
Right to license triggered upon successful data

- **Milestone-based Collaboration**

Conditional investment tied to defined results (e.g., pharmacodynamic efficacy, safety profile)

- **Sponsored Research Agreement (SRA)**

Industry-funded continuation of current preclinical work at the university
Potential for first negotiation rights

- **Spin-off Participation Opportunity** *(if applicable)*

Potential equity position in future spin-off company
Early strategic involvement in shaping development and IP

Acknowledgements

Pascual Torres is a Beatriu de Pinós postodoctoral fellow (2023 BP 00144), funded by the Department of Research and Universities (Generalitat de Catalunya).
Email: pascual.torres@udl.cat