IMPERIAL

Seeing the unseen: prions with a new light

Engineering human cells to propagate fluorescent prions in ovPrP-Glow line for live monitoring of prion infection with high-resolution in situ prion structure determination.

Ellie Hanzi
11/07/2026

PrP^C misfolding and aggregation dynamics

Prion propagation induced by exposure to existing aggregates

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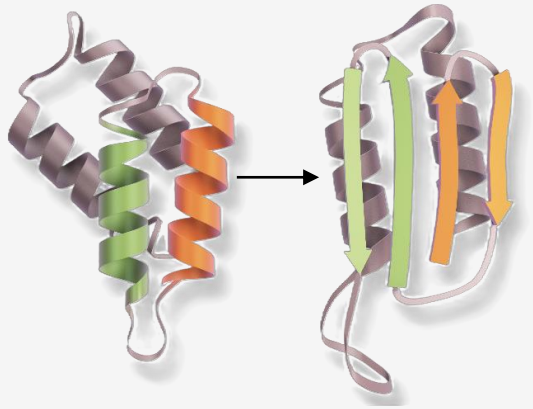
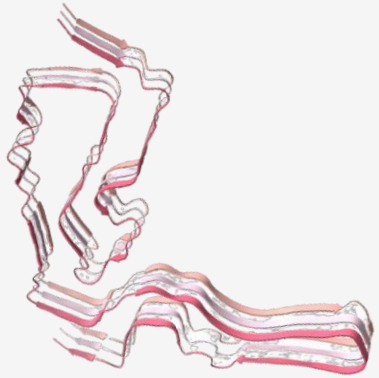
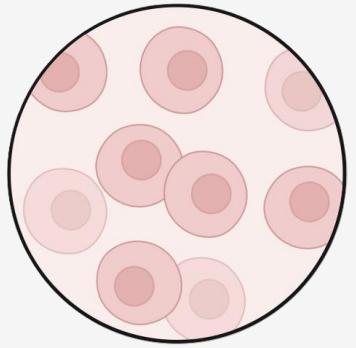
Mechanism through seeded polymerisation and fragmentation

→

When, where, and how within the cell?

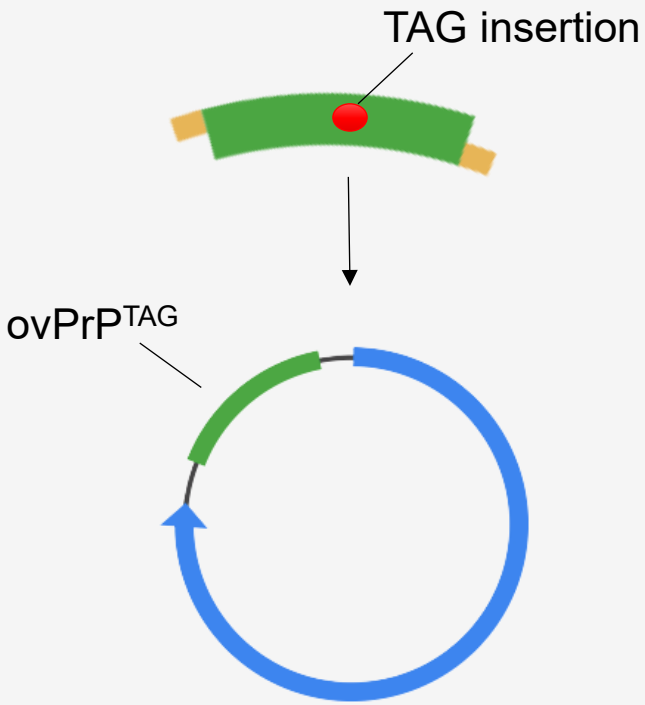




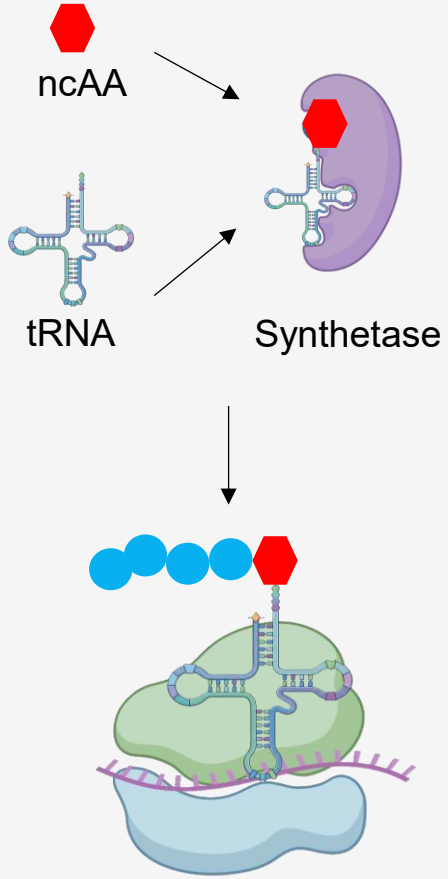


Developing genetic code expansion and bio-orthogonal labelling in sheep prion protein

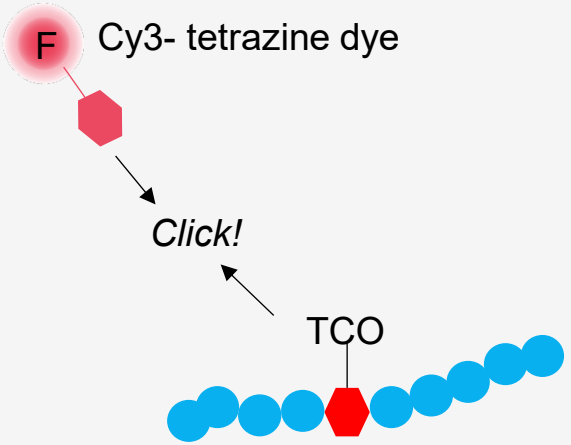
1 Construct design for ovPrP^{TAG}



2 Genetic code expansion

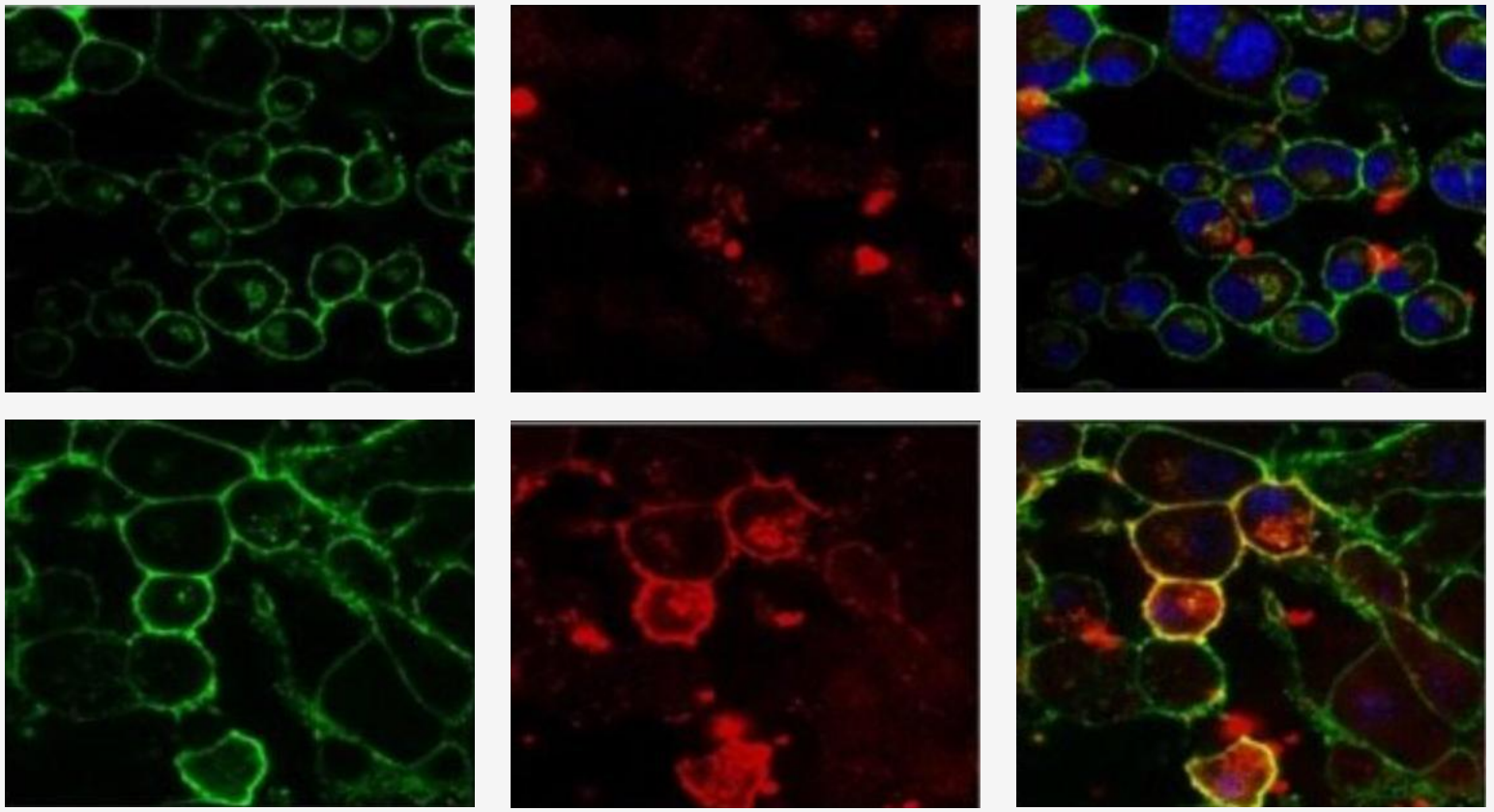


3 Bio-orthogonal labelling

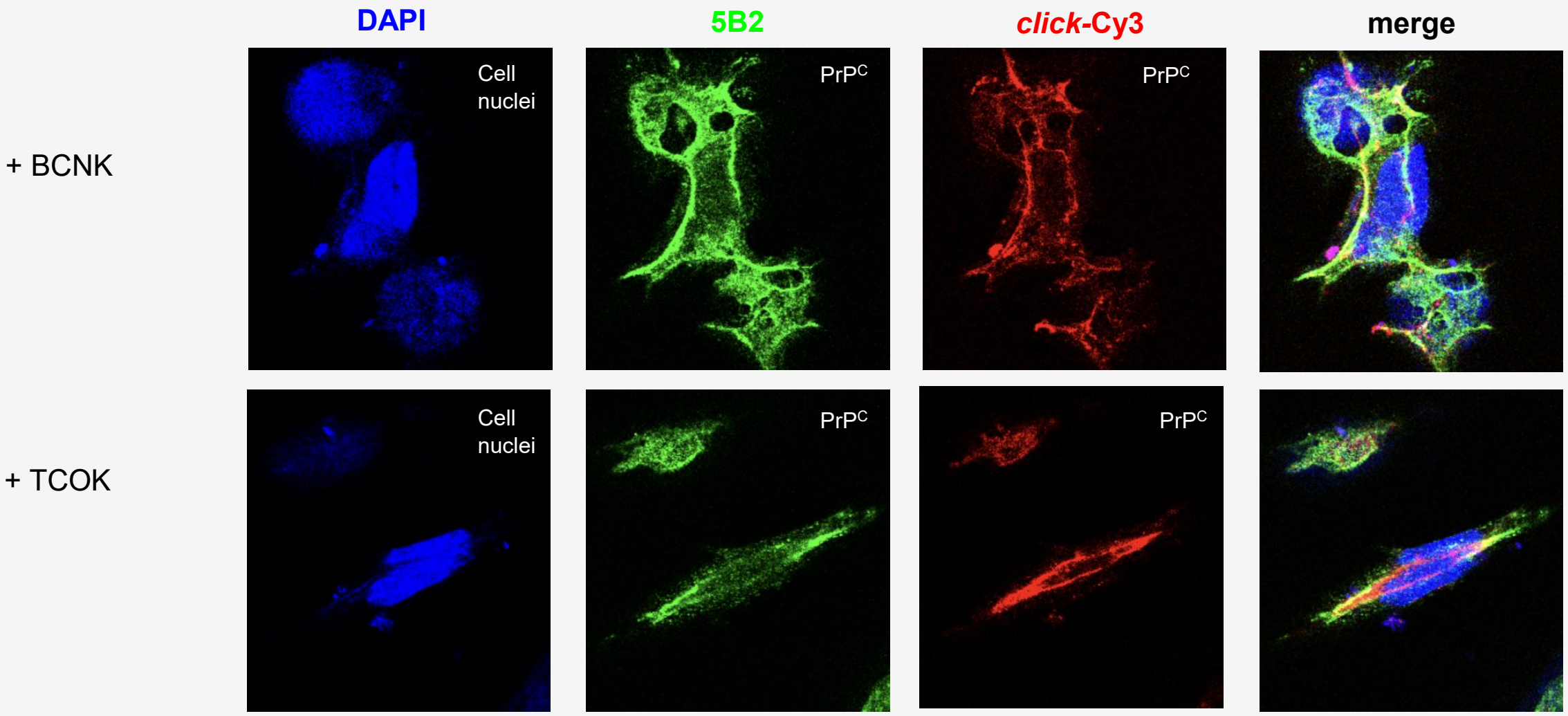


Pilot GCE system in mouse prion protein

Tom Trainer



Genetic code expansion of ovine PrP^C for ovPrP-Glow



LN229$^{\Delta PRNP}$ cells under confocal microscopy; fixed

Future directions

After the successful transfection of modified sheep prion protein, we know we can move forward to develop this system for tracking prion propagation dynamics.

Generation of stable cell line producing clickable ovPrP^{TAG}

Live cell single molecule studies of PrP^{C} and prion-binding factors

Cryo-CLEM of infected cells

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Conclusions and summary

- The traditional labelling of proteins in cells isn't compatible for the study of prion propagation: bulky fluorescent dyes interfere with prion protein conversion into its pathogenic form.
- Here, I show that a single amino acid within the prion protein can be modified to produce a fluorescent (glowing) prion protein in human cells.
- Such a minimal modification aims to enable the live tracking of prion propagation for a better understanding of the molecular mechanisms driving prion disease.
- The future research will aim to identify and validate key molecular players in human cells that facilitate prion propagation as potential therapeutic targets.