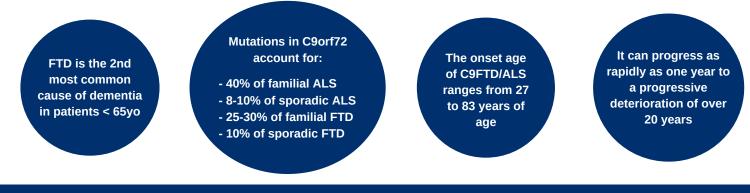


A novel C9FTD/ALS therapy

Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD) are intrinsically related and C9orf72-mediated ALS and FTD (C9FTD/ALS) is the most common hereditary cause. Whereas FTD is a cognitive and behavioural disorder characterized by changes to personality and language skills, ALS is a neuromuscular disease, which leads to paralysis and movement disorders to eventually respiratory failure.



The target: C9orf72 gene

- Abundant in neurons in the cerebral cortex and in motor neurons
- MoA: loss of function, toxic gain of function and toxic dipeptide repeats proteins (DRP) from GGGGCC hexanucleotide repeats
- Unclear threshold of number of repeats to cause FTD/ALS
- Antisense and sense transcripts lead to five different types of DRPs, all of them related to pathology
- Unclear whether pathology is only related to the final toxic repeats and/or to the transcripts themselves

Therapeutic approaches and limitations



Our approach: An effective RNA targeting therapy based on CasRx (Cas13d - RNA binding) and gRNAs for both sense and antisense C9orf72 hexanucleotide repeat transcripts









