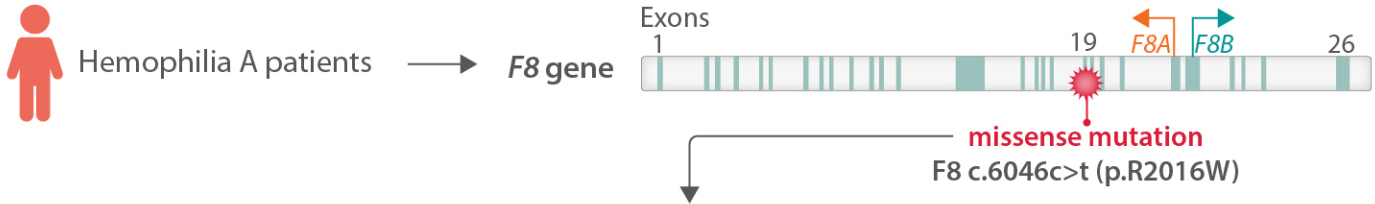


# Quantitative and qualitative insights into the potential pleiotropic effect of F8 missense mutations causing hemophilia A



## Factor VIII protein

- Impaired secreted levels (11.0±0.4% of wild-type)
- Impaired functional levels (6.0±2.9%)

## F8 mRNA

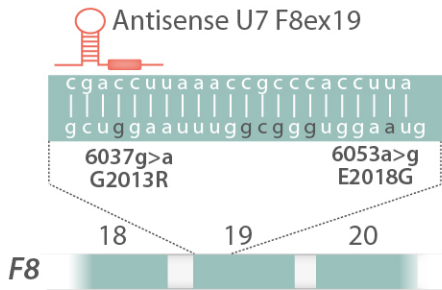
- Decreased correct splicing to 70±5%
- Impaired activity (4.2±2%)

## c.6037g>a (p.G2013R)

- Reduced exon inclusion to 41±3%
- Reduced antigen (7.0±0.9%) and activity (8.4±0.8%)

## c.6053a>g (p.E2018G)

- Reduced exon inclusion to 28±2%
- Produced dysfunctional antigen (69.0±18.1%) and activity (19.4±2.3%)



Differentially altered mRNA and protein patterns produce a gradient of residual activity, and clarify genotype-phenotype relationships