Constitutional SAMD9L mutations cause familial myelodysplastic syndrome and transient monosomy 7

From 4 unrelated pedigrees with myelodysplastic syndrome and loss of 7/7q
Median age 2.1 (1-42) years
Thrombocytopenia w/ or w/o cytopenia and hypocellular marrow

Heterozygous missense mutations in SAMD9L gene (7q21)

Mechanisms of clonal escape from SAMD9L mutations
- Monosomy 7 (n=7)
- Acquired truncated SAMD9L variants (n=2)
- Deletion 7q (n=1)
- UPD7q (n=2)

MDS development
Benign outcome and normal hematopoiesis

→ Description of the somatic landscape likely contributing to MDS progression
→ Observation of transient monosomy 7
→ Occurrence of non random revertant mosaicism leading to complete hematological recovery

Pastor et al., Haematologica, 2018