# VON WILLEBRAND FACTOR ANTIGEN AND AGE EXPLAIN VARIATION IN BASELINE FVIII:C

among persons with nonsevere haemophilia A with the same *F8* genotype (Arg593Cys and Asn618Ser)

## Conclusion

- **Age, *F8* mutation, VWF:Ag and haemophilia treatment center together explain 61% of the variance in baseline FVIII:C.**
- **In persons with haemophilia with the same *F8* mutation, the determinants age, VWF:Ag and haemophilia treatment center contribute to baseline FVIII:C to variable extends.**
- **This suggests that yet unknown factors influence FVIII:C in nonsevere haemophilia A.**

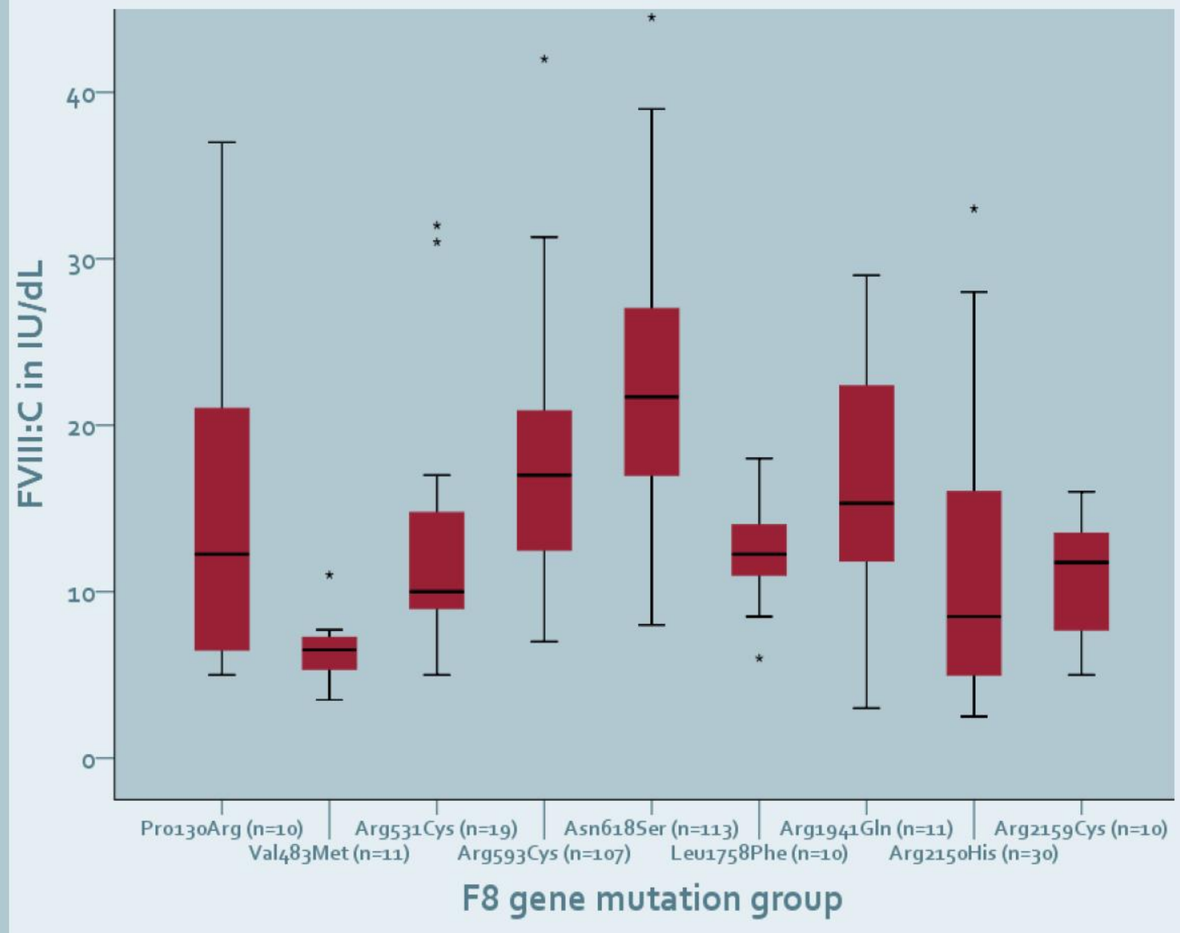
## Objectives

- The aim of the current study was to identify the determinants of baseline FVIII:C.
- Nonsevere haemophilia A (baseline FVIII:C, 2-40 IU/dL) is caused by a mutation in the *F8* gene.
- Great variation of baseline FVIII:C in persons with haemophilia with the same mutation was observed in the INSIGHT cohort, a large source population of 2,709 persons with nonsevere haemophilia A.
- There is limited knowledge on the factors determining the variation in baseline FVIII:C.

## Results

- We identified nine missense mutations present in at least 10 individuals in a total population of 321 persons with haemophilia, displaying 667 FVIII:C measurements (*Fig 1.*).
- Age, *F8* mutation, VWF:Ag and haemophilia treatment center together explained 61% of the variation in baseline FVIII:C.
- Within the largest mutation group Asn618Ser (n=113) only 21% of the variance in baseline FVIII:C was explained by the combined potential determinants (*Tab 1.*).
- The determinants explained 34% of the variance in baseline FVIII:C in Arg593Cys (n=107) (*Tab 1.*).

**Fig 1.** Great variation in baseline FVIII:C within the same mutation groups




**Tab 1.** Explained variation in the two largest mutation groups

| | Asn618Ser (n=113) | Arg593Cys (n=107) |
|---|---|---|
| VWF:Ag | **p<0,000** | **p<0,008** |
| VWF:Act | p=0,951 | p=0,430 |
| Age at measurement | **p<0,000** | p=0,104 |
| **Explained variation by combined determinants (R square, adjusted for haemophilia treatment center)** | **21%** | **34%** |

## Methods

- We analyzed clinical data of persons with nonsevere haemophilia A, treated between 1980-2013 in European haemophilia treatment centers participating in the INSIGHT/RISE consortium.
- We performed analyses on mutations that were present in ≥10 individuals (n=321). Age (at FVIII:C measurement), *F8* gene mutation, VWF:Ag and VWF:Act were analyzed as potential determinants by multivariate regression analyses. We corrected for haemophilia treatment center.


ZonMw
The Netherlands Organization for Health Research and Development
CSL Behring
Biotherapies for Life™



Janneke I. Loomans,[1] Alice S. van Velzen,[1] Corien L. Eckhardt,[1] Marjolein Peters,[1] Jan Astermark,[2] Paul P. Brons,[3] Giancarlo Castaman,[4] Marjon H. Cnossen,[5] Natasja Dors,[6] Carmen Escuriola-Ettingshausen,[7] Karly Hamulyak,[8] Daniel P. Hart,[9] Charles R.M. Hay,[10] Saturnino Haya,[11] Waander L. van Heerde,[3] Cedric Hermans,[12] Margaretha Holmström,[13] Victor Jimenez-Yuste,[14] Russell D. Keenan,[15] Robert Klamroth,[16] Christoph Königs,[17] Marieke J.H.A. Kruip,[5] Britta A.P. Laros-van Gorkom,[3] Frank W.G. Leebeek,[5] Ri Liesner,[18] Anne Mäkipernaa,[19] Christoph Male,[20] Evelien Mauser-Bunschoten,[21] Maria G. Mazzucconi,[22] Simon McRae,[23] Karina Meijer,[24] Michael Mitchell,[25] Massimo Morfini,[26] Marten Nijziel,[27] Johannes Oldenburg,[28] Kathelijne Peerlinck,[29] Pia Petrini,[13] Helen Platokouki,[30] Savita Rangarajan,[25] Sylvia E. Reitter-Pfoertner,[19] Elena Santagostino,[31] Piercarla Schinco,[32] Frans J. Smiers,[33] Berthold Siegmund,[34] Annarita Tagliaferri,[35] Thynn T. Yee,[36] Pieter Willem Kamphuisen,[23] Johanna G. van der Bom,[37] and Karin Fijnvandraat,[1] for the INSIGHT/RISE Study group.

[1]Academic Medical Center, Amsterdam, the Netherlands; [2]Skåne University Hospital, Malmö, Sweden; [3]Radboud University Medical Center, Nijmegen, the Netherlands; [4]San Bortolo Hospital, Vicenza, Italy; [5]Erasmus University Medical Center, Rotterdam, the Netherlands; [6]Catharina Hospital, Eindhoven, the Netherlands; [7]Haemophilia Centre Rhein-Main, Darmstadt, Germany; [8]Maastricht University Medical Center, Maastricht, the Netherlands; [9]Royal London Hospital, Barts and The London School of Medicine and Dentistry, London, the United Kingdom; [10]Manchester Royal Infirmary, Manchester, the United Kingdom; [11]University Hospital la Fe, Valencia, Spain; [12]St-Luc University Hospital, Brussels, Belgium; [13]Karolinska University Hospital, Stockholm, Sweden; [14]University Hospital La Paz and Autonoma University, Madrid, Spain; [15]Alderhey Childrens Hospital, Liverpool, the United Kingdom; [16]Vivantes Klinikum im Friedrichshain, Berlin, Germany; [17]JW Goethe University Hospital, Frankfurt, Germany; [18]Great Ormond Street NHS Trust, London, the United Kingdom; [19]Children's Hospital, Helsinki University Central Hospital, Helsinki, Finland; [20]Medical University of Vienna, Vienna, Austria; [21]University Medical Center Utrecht, Utrecht, the Netherlands; [22]Sapienza University of Rome, Rome, Italy; [23]Royal Adelaide Hospital, Adelaide, Australia; [24]University Medical Center Groningen, Groningen, the Netherlands; [25]Guy's and St. Thomas' NHS Foundation Trust, London, the United Kingdom; [26]Azienda University Hospital Careggi, Florence, Italy; [27]Maxima Medical Center, Eindhoven/Veldhoven, the Netherlands; [28]University Clinic of Bonn, Bonn, Germany; [29]University of Leuven, Leuven, Belgium; [30]Aghia Sofia Children's Hospital, Athens, Greece; [31]Ospedale Maggiore Policlinico, Fondazione IRCCS Ca' Granda, Milan, Italy; [32]San Giovanni Battista "Molinette" Hospital, Turin, Italy; [33]Leiden University Hospital, Leiden, the Netherlands; [34]Raphaelsklinik, Munster, Germany; [35]University Hospital of Parma, Parma, Italy; [36]Royal Free Hospital, London, the United Kingdom; [37]Sanquin Research, Leiden, the Netherlands.



WFH2014 81--P-T
Mild Hemophilia
Janneke Loomans
DOI: 10.3252/pso.eu.WFH2014.2014
Poster presented at: WFH 2014 World Congress, Melbourne, Australia, May 11-15
PosterSessionOnline.com