Dissecting the pathophysiology of immune thrombotic thrombocytopenic purpura: interplay between genes and environmental triggers

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Published in Haematologica 2018;103(7):1099-1109.

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doi:10.3324/haematol.2020.278244

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On page 1100-1101 we would like to change the sentence:

"The clinical significance of the restricted VH1-69 germline gene segment has been observed in neutralizing Abs directed toward a highly conserved region in the hemagglutinin ectodomain of the influenza virus[35] and in patients with B-cell lymphoma after chronic hepatitis C infection.[36]"

to:

"Antibodies directed towards the ectodomain of hemagglutinin of the influenza virus as well as hepatitis C virus are also frequently encoded by VH1-69 germline gene segments.[35,36]"

On page 1103 we would like to change the sentence:

"Activation of ADAMTS13-specific CD4+ T cells requires uptake of ADAMTS13 by antigen-presenting cells (APCs) and presentation of ADAMTS13-derived peptides on HLA molecules. As the HLA-DRB1*11 was identified as a risk factor for the development of iTTP, investigation of ADAMTS13-derived peptides that are preferentially presented on MHC class II of healthy individuals positive for this allele was performed.[66]"

to:

"Proteolytic degradation of endocytosed ADAMTS13 in endo-lysosomal compartments in antigen-presenting cells has been shown to result in presentation of ADAMTS13-derived peptides on MHC class II molecules. It has been well-established that HLA-DRB1*11 is a risk factor for the development of iTTP.[57,58] This prompted us to explore the repertoire of ADAMTS13-derived peptides presented on this risk allele for iTTP.[66] "

On page 1105 we would like to change the sentence:

"Raised VWF levels are required to induce TTP in Adamts13$^{-/-}$ mice, but varying the concentration between 20 and 120 U/mL does not appear to affect the occurrence or severity of the disease, suggesting that a threshold level of VWF is sufficient, and that higher levels confer little additional risk. However, humans appear to be more sensitive to changes in VWF levels than mice. Women with inherited ADAMTS13 deficiency frequently develop TTP during pregnancy, which probably results from the progressive increase in VWF levels throughout the gestation period. Moreover, obese individuals have higher levels of VWF, providing further evidence for an association between obesity and TTP. Thus, changes in VWF secretion, multimer distribution, and plasma level may trigger TTP.[78]"

to:

"A threshold level of VWF has been suggested to promote shiga toxin-induced TTP in *Adamts13*$^{-/-}$ mice.[78] During pregnancy VWF levels increase progressively; this may contribute to the development of microvascular thrombosis in pregnant woman with congenital or immune-mediated TTP.[78] Moreover, obese individuals have higher levels of VWF, providing further evidence for an association between obesity and TTP. These findings raise the possibility that elevated levels of VWF may contribute to the onset of TTP in various physiological or clinical conditions.[78]"