Pediatric RESEARCH

IMAGE

Insights Image for "Dystrophin deficiency promotes leukocyte recruitment in mdx mice"

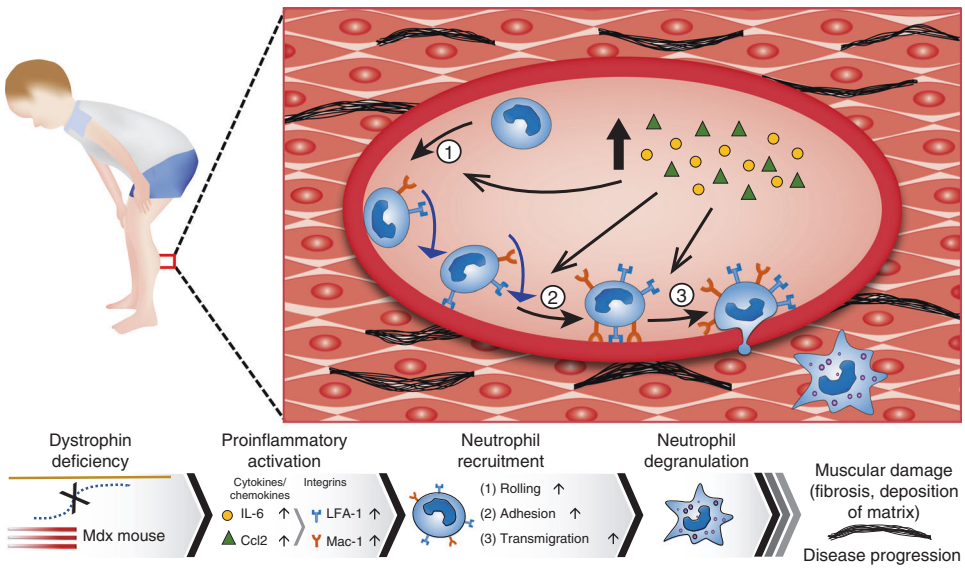
Simon Alexander Kranig[1], Raphaela Tschada[1], Maylis Braun[1], Johannes Pöschl[1], David Frommhold[2] and Hannes Hudalla[1]

Pediatric Research (2020) 87:798; https://doi.org/10.1038/s41390-019-0659-2

The illustration depicts a mechanism by which neutrophil recruitment may contribute to disease progression in Duchenne Muscular Dystrophy (DMD), as proposed by our group.[1] Neutrophils are recruited to muscle tissue in post-capillary venules, following a defined cascade of events. In the cremaster muscle of dystrophin-deficient mdx mice (C57BL/10ScSn-*Dmd*^{mdx}), neutrophils show enhanced recruitment to muscle tissue in intravital microscopy (IVM). Mdx mice show increased circulating levels of IL-6 an Ccl2, partially accounting for the upregulation of integrins like Lymphocyte function-associated antigen 1 (LFA-1) and Macrophage-1 antigen (Mac-1) on dystrophin deficient neutrophils. Integrin upregulation, cytokine and chemokine induction and potential endothelial activation contribute to enhanced leukocyte capture and rolling (assessed as rolling flux fraction, (1) and leukocyte adherence (2) in mdx mice. Eventually, transmigration and infiltration of surrounding muscle tissue is increased in the context of dystrophin deficiency (3). It is known that neutrophil degranulation in skeletal muscle then contributes to tissue inflammation, fibrosis and matrix deposition. The lower panel describes the individual events of this mechanism in detail. We suggest that enhanced neutrophil recruitment may contribute to disease progression in DMD patients.

REFERENCE

1. Kranig, S.A. et al. Dystrophin deficiency promotes leukocyte recruitment in mdx mice. *Pediatr. Res.* **86**, 188–194 (2019).



[1]Department of Neonatology, Heidelberg University Children's Hospital, 69120 Heidelberg, Germany and [2]Klinik für Kinderheilkunde und Jugendmedizin, 87700 Memmingen, Germany
Correspondence: Hannes Hudalla (Hannes.Hudalla@med.uni-heidelberg.de)

Received: 14 October 2019 Accepted: 14 October 2019
Published online: 4 November 2019