

Role of Aquaporin-9 in inflammatory skin disease

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Aquaporins (AQPs, AQP0-12) are membrane water/glycerol channel proteins that participate in various cellular functions in many cell types. AQP9 is expressed in several immune cells including neutrophils; however, its role in cutaneous immune response remains unknown. Here we show the involvement of AQP9 in skin allergic inflammation using AQP9 knockout (AQP9^{-/-}) mice and the contact hypersensitivity (CHS) model.

First, AQP9^{-/-} mice showed impairment of CHS responses to hapten (DNFB) compared with wild-type (WT) mice. Adoptive transfer of AQP9^{-/-} LN cells into the ears of WT recipients resulted in impaired CHS response, indicating the defect of sensitization in AQP9^{-/-}. IL-17 production was decreased in AQP9^{-/-} compared with WT LN cells.

WT mice showed high neutrophil accumulation in LNs at 18 h after DNFB application, but it was abrogated in AQP9^{-/-} mice. In accordance, we found the attenuation of AQP9^{-/-} neutrophil migration to LNs after DNFB application. Furthermore, the neutrophil migration in response to CCR7 ligands was suppressed in AQP9^{-/-} using chemotaxis chambers.

Finally, we found that the administration of neutralizing antibody during the sensitization phase suppressed IL-17 production from LN cells as well as CHS response in WT mice, suggesting the implication of neutrophils for IL-17 production during the development of CHS.

These data suggest that AQP9-expressing neutrophils play an important role in the sensitization phase of CHS through their migration function.