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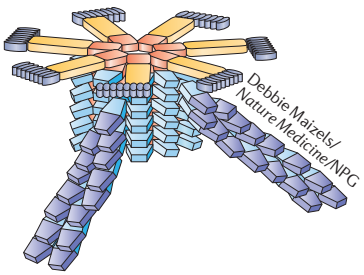
VASCULITIS SYNDROMES

Kawasaki disease is IL-1β-mediated

The calcium-mobilizing enzyme inositol-triphosphate 3-kinase C (ITPKC) has a key role in the immunopathogenesis of Kawasaki disease (KD), according to research just published in *The Journal of Immunology*.

The results of the study, which combined analyses of peripheral blood samples from 185 children with KD and mechanistic studies of the effects of *Itpkc* deficiency in a mouse model of KD, clearly show that ITPKC controls NLRP3 expression and activation via regulation of intracellular calcium levels, thereby promoting production of IL-1β and IL-18. Of note, this novel mechanism also accounts for the observed efficacy of rescue therapy with IL-1 blockers in children with treatment-refractory KD.



"A perfect storm of data led us to this specific project," comments Rae Yeung, the study's corresponding author, referring to the group's prior findings linking an IL-1β–IL-18 cytokine signature to NLPR3 inflammasome activation in KD, as well as the known role of calcium in regulation of the NLRP3 inflammasome and recent genetic data strongly associating *ITPKC* variants with susceptibility to and outcome of KD. "[However,] the paradigm shift [lay in] thinking of KD as an IL-1β-mediated disease," she continues. "We [have] identified regulation of calcium mobilization as fundamental to the underlying immunobiology of KD leading to this IL-1β signature, thus changing the way we think about KD," Yeung explains. The researchers hypothesize that an infectious or environmental trigger of KD in an individual with low ITPKC levels (*ITPKC* CC risk genotype) results in increased inflammasome activation and, potentially, refractory KD.

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ORIGINAL ARTICLE Alphonse, M. P. *et al.* Inositol-triphosphate 3-kinase C mediates inflammasome activation and treatment response in Kawasaki disease. *J. Immunol.* http://dx.doi.org/10.4049/jimmunol.1600388 (2016)