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A new look at caspase 12 research

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Inflammasomes are assemblies that are central to inflammatory responses. Dr. Lieselotte Vande Walle, Daniel Jiménez Fernández and colleagues from Prof. Mo Lamkanfi's group (VIB/UGent) shed new light on the function of caspase 12. In doing so, they have rid the field of a stubborn dogma, which held that caspase 12 was a negative regulator of inflammasomes. These novel insights pave the way for researchers to break from the route of existing research and identify the real physiological functions of caspase 12.

The VIB researchers have also pointed out that this will require a great deal of 're-researching'. The previously supposed roles of caspase 12—with more than 9,000 citations—in cell death and stress responses, malaria, sepsis etc. must be recalculated because they were often obtained on the basis of incorrect mouse models.

Prof. Mo Lamkanfi (VIB/UGent): "We have discovered that, in many cases, research into caspase 12 has been conducted on the basis of mouse models that knock out caspase 11, as well as caspase 12. It is impossible to extrapolate research results on the role of caspase 12 from this. We have now introduced new, selective caspase 12 KO mice that should enable us to trace the exact role of caspase 12."

Using these new mice, the Lamkanfi group showed that caspase-12 deficiency in both ex vivo-stimulated BMDMs and in in vivo-challenged mice failed to increase caspase-1 activation. Release of mature IL-1β and IL-18 by inflammasome pathways was consequently also not enhanced by deletion of caspase 12. Their findings show that

irrespective of caspase-11 expression status, caspase 12 doesn't act as a physiological dominant-negative regulator of caspase-1 activation and hence of inflammasomes.

More information: Lieselotte Vande Walle et al, Does caspase-12 suppress inflammasome activation?, *Nature* (2015). DOI: 10.1038/nature17649

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