Annexin A2 – friend or foe

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Annexin A2 knock-out mice are essentially healthy and viable, a feature of most annexin knock-out mice. If one assumes all genes to be essential (otherwise why would they be conserved in evolution), then the lack of overt phenotypes in annexin knock-out mice demands explanation. One possibility is functional redundancy between individual annexin family members, but in general there is little evidence i) that annexins have sufficiently overlapping activities that would permit such complementation of function, or ii) that targeted gene disruption of one annexin leads to changes in expression that might be expected in other annexins. Our studies in the annexin A2 knock-out mouse have revealed a role for this protein in retinal phagocytosis, such that the mutant mouse exhibits a delay in the uptake of shed photoreceptor outer segments following diurnal shedding. Despite this abnormality, the retina is not adversely affected in these mice, and indeed in the long term we observed that as these mice age their visual function is actually better than that of similarly aged littermates. This would indicate, surprisingly, that annexin A2 somehow contributes to the decline in visual function that accompanies ageing in all mammals. In a second study, we examined the effects of inducing diabetes in the annexin A2 knock-out mouse. Annexin A2 mice, when diabetic, develop a much more severe pathology than normal diabetic mice, attributable to defective kidney function and most likely linked to a role for annexin A2 in water reabsorption in the epithelial cells of the loop of Henlé. These mice succumb rapidly to the pathological consequence of diabetic nephropathy while their genetically normal diabetic littermates remain almost unaffected. Taken together, these studies suggest that in the mouse annexin A2 is actually both friend and foe, acting in a protective manner in the disease setting (diabetes), but contributing to the decline in sensory function in normal healthy ageing.