When immunity and extracellular matrix matter: repair and regenerative events after echinoderm arm injury

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Arm amputation in echinoderms is a traumatic event that removes differentiated body parts and damages all tissue types. Immediately after injury the repair phase begins. If phenomena typical of this phase, such as emergency reaction, inflammatory/immune response, wound closure and extracellular matrix (ECM) remodelling and deposition, do not properly occur, the following regenerative process may be prevented or ineffective.
In this study, the brittle star *Amphiura filiformis* (*Afi*) was used as model to investigate the main repair and regenerative events after arm injury, with a specific focus on the involvement of immune and ECM genes and proteins. In this perspective, both microscopy and molecular analyses were performed to highlight similarities and differences between regeneration-competent (*i.e.* echinoderms) and non-competent (*i.e.* mammals) animals.
Our microscopy results showed that both emergency reaction and re-epithelialisation are faster in brittle stars than in mammals. Fibrosis, *i.e.* over-deposition of ECM due to an exaggerated inflammatory reaction, is not detectable in echinoderms as, instead, described for mammals, suggesting that immunity modulation may facilitate subsequent regeneration. Our molecular analyses showed that *Afi-ficolin* (an important gene in the immune response) is expressed in the first phase after injury, whereas almost all the selected ECM genes are not expressed at early stage of regeneration, suggesting an activation delay that may be directly connected to their regeneration efficiency, as proposed for other echinoderms and in contrast to most vertebrates. Moreover, at advanced regenerative stages these same genes are differentially expressed, suggesting that the molecular regulation of ECM deposition/remodelling is different throughout re-growth.
Overall, our brittle star model shows similarities in terms of repair and regenerative events and timing with other echinoderm species already studied. However, differences emerge between echinoderms and mammals: indeed, all phenomena should occur following specific signals and timing to ensure effective regeneration after severe wounds. Further quantitative analyses will allow a better understanding of immune system and ECM contribution to brittle star arm regeneration and of the evolutionary implications on the regeneration competence widespread in the animal kingdom.