

## Talk 12

### Amyloid and allorecognition in the colonial ascidian *Botryllus schlosseri*

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Allorecognition, i.e., the ability of intraspecific nonself recognition is widely distributed among colonial, sessile marine organisms in the form of colony specificity. In the cosmopolitan compound ascidian *Botryllus schlosseri*, colony specificity is controlled by a highly polymorphic Fu/HC locus: two colonies sharing at least one allele at the Fu/HC locus can fuse into a chimeric colony; if no alleles are shared, a typical inflammatory reaction occurs, with the recruitment of a specific hemocyte type, the cytotoxic morula cells (MCs), inside the tips of the ampullae (the blind termini of the tunic vasculature) extending towards the alien colony, their extravasation in the tunic and their final degranulation. As a consequence of allorecognition, necrotic, melanic spots (points of rejection; PORs) form along the contact border, due to the release, by MCs, of their granular content, mainly represented by quinones, polyphenols and the enzyme phenoloxidase (PO), upon the perception of the allogeneic humoral factors diffusing from the alien colony through the partially fused tunics. It is remarkable that the deposition of melanin and the cell death is confined to the immediate outside of the ampullar tips, suggesting that the diffusion of PO and the products of its activity are, in some way, prevented in order to limit cytotoxicity to the immediate neighborhood of the contact region. In this context, we looked for factors released by MCs that could limit the spreading of cytotoxicity and melanisation.

We found that MCs share with vertebrate melanocytes similar packaging of melanin precursors, entrapped in a 3D scaffold of amyloid fibrils. They contribute to form the electron dense content of MC granules that, after stimulation, flake off and is released in the surrounding medium. Released amyloid fibrils limit the diffusion of the produced melanin.

The search for genes and factor controlling both melanogenesis and amyloidogenesis, revealed an evolutionary conserved machinery involved in the processes and an unexpected cross talk between the two *Botryllus* immunocyte types, i.e., phagocytes and MCs. Furthermore, this work confirms the physiological role of amyloid in tunicate immunity.

