

REPORT OF MEETING

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Organizers: **G Scapigliati, AM Fausto, M Mazzini, N Romano, F Buonocore, S Picchietti, MC Belardinelli**

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Allorecognition in the ascidian *Botryllus schlosseri*: the importance of amyloid.

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In the compound ascidian *Botryllus schlosseri*, allorecognition manifests primarily as colony specificity, controlled by a highly polymorphic Fu/HC locus, so that contacting colonies sharing at least one allele at the Fu/HC locus can fuse into a chimeric colony; if no alleles are shared, a typical inflammation 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 with the consequent release of factors inducing autocrine and paracrine cell and the formation of necrotic, melanic spots (points of rejection; PORs) along the contact border.

MCs are the first cells to sense nonself and are the source of cytokines that induce the recruitment of immunocytes at the inflammatory sites and the activation of phagocytes required for the clearance of foreign material. MCs store quinones, polyphenols and the enzyme phenoloxidase (PO) inside their granules, representing their cytotoxic potential. Although PO, quinones and polyphenols are soluble factors, 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 the enzyme and the products of its activity is, in some way, prevented in order to limit cytotoxicity to the immediate neighbourhood of degranulating MCs. With this idea in mind, we looked for factors released by MCs that could limit the spreading of cytotoxicity and melanisation. We found that MCs contain amyloid inside their granules and that amyloid fibrils are released in the surrounding medium upon MC degranulation forming a net-like scaffold entrapping PO and melanin, thus limiting their diffusion. In addition, 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. This work represents the first demonstration of a physiological role of amyloid in protochordata immunity.