

ImmunoTools *special* Award 2018



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Ability of the peripheral glial cells (Schwann cells) to drive the inflammatory response during nerve regeneration: role of alpha-7 nicotinic receptor

Peripheral Nervous System (PNS) has an intrinsic ability of regeneration. When a nerve is damaged, the distal stump degenerates in a process called Wallerian Degeneration, whereas the proximal stump can regenerate to reach the original target. Schwann cells (SCs) form the myelin sheath in the PNS and, after a damage, they de-differentiate, assuming a phenotype known as Repair Schwann Cells: they up-regulate genes involved in proliferation, production of cytokines and growth factors to produce an anti-inflammatory environment that supports the peripheral nerve regeneration: For these reasons, SCs could be good candidate for a cell therapy supporting nerve regeneration.

Cholinergic system plays an important role in this process, via muscarinic receptors: Schwann cells express all the subtypes (M1, M2, M3, M4). Mainly, the activation of the muscarinic subtype M2 activity modulates the expression of growth factors, as NGF, BDNF and GDNF, and early genes involved in SC proliferation as C-jun. Recently, in our lab, we found that Schwann cells up-regulate the nicotinic receptor subtype $\alpha 7$ when located in the pro-inflammatory environment. Our aim is to investigate the functions of this receptor, underlining its possible anti-inflammatory function and supporting nerve regeneration. Nowadays, considering that SCs have some limits as low proliferative rate and difficulty to collect, scientific research pays attention on alternative cell therapies. The best candidate seems to be Mesenchymal Stem Cell derived from adipose tissue (uASC) that can be differentiated in a phenotype Schwann-Like (dASC). In our laboratory, we found both uASCs and dASCs express the nicotinic subtype receptor $\alpha 7$. Even in this case, our aim will be to investigate the role of this receptor in the modulation of processes like proliferation, migration, production and modulation of pro-inflammatory cytokines.

Thus to study the role of $\alpha 7$ nicotinic receptors in peripheral nerve regeneration we 'll use rat Schwann cell derived from sciatic nerve and dASC derived from rat and human mesenchymal stem cells. The cultures, will be stimulated by inflammatory molecules such as Bradykinin and the $\alpha 7$ agonist (R)-(-)-3-methoxy-1-oxa-2,7-diaza-7,10-ethanspiro[4.5]dec-2-ene sesquifumarate [(R)-ICH3] will be used to study the effects mediated by the selective activation of this receptor.

To maintain in culture the dASC are also required several growth factors as Fibroblast Growth Factor (FGF), Platelet Derived Growth Factor (PDGF), Neuregulin (NRG) and Forskolin (FSK).

ImmunoTools *special* AWARD for **Ada Maria Tata** includes 16 reagents

recombinant human cytokines: rh FGF-b/FGF2, rh Neuregulin-1a, rh Neuregulin-1b, rh beta NGF, rh PDGF-AA, rh PDGF-BB, rh SDF-1a/CXCL12a, rh SDF-1b/CXCL12b

human ELISA-set (for one 96 plate): human TNF-a and human IL-6

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