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Iemma Rocco Stefano et al., J Dementia Care 2018, Volume 4
DOI: 10.4172/2471-4372-C4-018

Anti-inflammatory property of acetylcholine against monomeric C-reactive protein on differentiated human U937 macrophage-like cells

Iemma Rocco Stefano and Mark Slevin
Manchester Metropolitan University, UK

Introduction & Aim: Ischemic stroke increases the risk of developing vascular dementia. C-Reactive Protein (CRP) is an acute phase protein which on tissue contact become dissociated into free sub-units or monomeric CRP (mCRP) concomitantly increasing which increases its pro-inflammatory and adhesion properties. Previous studies show that mCRP accumulated in the infarcted core and peri-infarcted zone after ischemic stroke and promoted the progression of dementia. Thus, here we investigated whether the use of an anti-mCRP antibody or appropriately structured small molecule could block mCRP induced inflammatory activity.

Method: The dot blot technique was used to evaluate potential interactions between mCRP and 3 Small Molecular Compounds (SMC) (acetylcholine, tacrine and nicotine). Cell viability assays were performed with the objective to determine if these compounds showed any cytotoxic effects that could lead to cell death on differentiated human U937 macrophage-like cells. Cells were stimulated with mCRP and the levels of cytokines in cell culture supernatant were determined by Enzyme-Linked Immunosorbent Assay (ELISA). One monoclonal anti-mCRP antibody (3H12) and the three SMC were tested for their anti- inflammatory activity after 2-hour pre-treatment. The relevant inflammatory signaling pathways were examined by Western blotting.

Result: mCRP increased the concentrations of Tumor Necrosis Factors-α (TNF-α) and interleukin-6 (IL-6) but not IL-10. 2-hour pre-treatment with acetylcholine significantly inhibited TNF-α release induced by mCRP (acetylcholine: 73.4% reduction compared to mCRP, $P<0.001$). Acetylcholine also decreased IL-6 production by mCRP by 66.74% ($P<0.001$). Western blotting revealed that acetylcholine inhibited the NF-kBp65 activation and p38 phosphorylation by mCRP.

Conclusion: This study demonstrated that mCRP has a potent pro-inflammatory activity and acetylcholine inhibited its pro-inflammatory activity by down-regulating NF-kB p65 and MAPK p38 signaling pathways. mCRP might serve as a promising new target for the prevention and treatment of vascular dementia.

Biography

Iemma Rocco Stefano is currently working at the Manchester Metropolitan University, under the supervision of Professor Mark Slevin. He holds a master's degree on Adapted Physical Activity and another Master's degree (120 ECTS) on Neurorehabilitation. He possesses a strong background in neuroscience, biology, anatomy, physiology, neurophysiology of different problems associated with the central nervous system.

rocco.iemma@stu.mmu.ac.uk

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