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EFFECTS OF RESVERATROL AND A NOVEL RESVERATROL-SALICYLATE HYBRID MOLECULE ON ACTIVATION OF HUMAN CD4+ T- CELLS

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Introduction: T-cells are assumed to be crucially involved in the pathogenesis of systemic autoimmune diseases such as rheumatoid arthritis (RA). Consequently, substances modulating T-cell activation may have therapeutic benefit in RA and related rheumatic diseases. Resveratrol is a natural occuring polyphenol mainly produced in plants. The beneficial effects of resveratrol are due to its anti-inflammatory, anti-carcinogenic and anti-oxidant activities.

Objectives: To compare the effects of resveratrol and a novel resveratrol-salicylate hybrid molecule termed C-10 (Aldawsari FS et al, 2016) on human $CD4^+$ T-cells .

Methods: $CD4^+$ T-cells were isolated from healthy donors and pre-incubated with different concentrations of resveratrol or C-10 before being stimulated with anti-CD3/anti-CD28 antibodies. After 24h and 72h, respectively, cell culture supernatants were harvested and IL-2, IFN-γ and TNF-α release was quantified by ELISA. Proliferation rate was measured by thymidine incorporation. In addition, the up-regulation of the early activation markers CD25, CD69, CD71 and CD98 was analyzed and phosphorylation of signal transduction molecules were determined by western blot and/or flow cytometry.

Results: Inhibition of IL-2, IFN-γ and particularly TNF-α release was significantly more effective when the cells were treated with C-10 as compared to resveratrol. Moreover, the proliferation rate was significantly more decreased in the presence of C-10. The expression of CD25, CD69, CD71 and CD98hc was reduced to a similar degree by both compounds. Furthermore, phosphorylation of Akt and STAT-5 was substantially attenuated by C-10 and to a lesser degree also by resveratrol. All T cell subsets investigated (Th1, Th2, Th17) were affected at a similar degree but the most pronounced effect was seen in naïve T cells.

Conclusions: Our data demonstrate that C-10 suppressed cytokine secretion and proliferation more effectively than resveratrol. Both compounds influence the phosphorylation of important signalling molecules. The effect exerted on STAT-5 activation may be the key mechanism for inhibition of T cell activation. Thus, the resveratrol-salicylate hybrid molecule C-10 might be considered a candidate drug for treatment of RA and other T-cell driven autoimmune diseases.

References:

Aldawsari FS, Aguiar RP, Wiirzler LA, Aguayo-Ortiz R, Aljuhani N, Cuman RK, Medina-Franco JL, Siraki AG, Velázquez-Martínez CA.Anti-inflammatory and antioxidant properties of a novel resveratrol-salicylate hybrid analog.Bioorg Med Chem Lett. 2016 Mar 1;26(5):1411-5.

Disclosure of Interest: None declared