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Ex-vivo study of extracorporeal photochemotherapy effects on immune system: early experience in healthy controls and a multiple sclerosis patient.

Rigolio R.[1], Perseghin P.[2], Petersson J.[3], Jonsson S.[4], Biffi A.[1], Cavaletti G.*[1], Cilio C.M.[5]

- [1]Università di Milano-Bicocca, Dipartimento di Neuroscienze e Tecnologie Biomediche, Monza, Italy ~ Monza - [2] Ospedale S. Gerardo dei Tintori, Dipartimento di Patologia Clinica, Unità di Aferesi e Nuove Tecnologie Trasfusionali, Monza, Italy ~ Monza - [3]Malmö University Hospital, Neurological Clinic, Malmö, Sweden ~ Malmö - [4]Malmö University Hospital, Haemoimmunotherapy Unit, Malmö, Sweden ~ Malmö - [5]Lund University, Malmö University Hospital, Department of Clinical Sciences,Cellular Autoimmunity Unit, Malmö, Sweden ~ Malmö

Extracorporeal photochemotherapy (ECP) is a procedure effective in the treatment of several human T-cell mediated diseases. During ECP treatment the patient's blood is processed by means of a cell separator to collect leukocytes (leukapheresis), mostly lymphocytes and monocytes (PBMC), which are then added with the photoactive drug 8-methoxypsoralen (8-MOP), exposed to ultraviolet-A light (UV-A) and reinfused into the patient. Even if the mechanisms of action of ECP remain elusive, it has been shown that it has an in-vivo immunomodulatory effect in experimental ellergic encephalomyelitis (EAE) and in a small pilot study in multiple sclerosis (MS) patients.
It has been suggested that during ECP not only UV-A irradiation but also the environmental condition changes may be relevant, an aspect which has never been investigated in detail. Therefore, we developed a new bench device which reliably mimics ex-vivo the complete ECP cycle and we investigated the effect of 8-MOP, UV-A and their combination on the synthesis of IFN-gamma, IL-2 and TNF-alpha on healthy controls and a MS patient.
PBMC were collected and treated with 8-MOP and/or UV-A under the same conditions used for the ECP therapy. PBMC were polyclonally stimulated with phorbol 12-myristate 13-acetate (PMA) and ionomycin in the presence of Brefeldin A (BFA) to prevent newly synthesized cytokine egression. Intracellular pro-inflammatory cytokines produced by activated T-lymphocytes were evaluated.
We observed a significant decrease in activated CD4+ and CD8+ T-lymphocytes producing cytokines after UV-A irradiation and a further decrease in the presence of 8-MOP + UV-A.
The decrease in cytokines production seemed to be both cytokine- and cell type-related. In fact TNF-alpha production was reduced to a lesser extent than IFN-gamma and IL-2 ones by both UV-A and the co-treatment, while CD4+ T-cells seemed to be more sensitive than CD8+ lymphocytes when IFN-gamma and IL-2 production was considered. Both T-cell population showed similar behaviour when TNF-alpha production was evaluated.
8-MOP and UV-A co-treatment affected T-lymphocytes activation after polyclonal stimulation and. reduced IFN-gamma, IL-2 and TNF-alpha production with different extent among the cytokines considered.
Following this preliminary experience this ex-vivo protocol will be used to extend the determinations in the EAE model and to reproduce these observations in a larger series of healthy controls and MS patients.