Evaluation of biological activities of highly diluted nucleotide sequences by using cellular models

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ABSTRACT

Background: highly diluted specific nucleic acids (SNA®), designed to modulate viral and cytokine genes expression, are currently used in Micro-Immunotherapy to treat viral infections and immune disorders. Although some preliminary studies have showed clinical benefit of these homeopathic preparations [1], no experimental data are available to explain their mechanism of action.

Aims: to investigate the in vitro effect of two sets of highly diluted (HD) SNA targeting i) latent/lytic Epstein-Barr virus (SNA EBV) and ii) TNF-α and its receptor p55 involved in rheumatoid arthritis (SNA RA) on cellular models.

Methodology: serial homeopathic dilutions of SNA EBV and SNA RA (15cH-18cH) were tested on a EBV-positive B-lymphoblastoid (B95-8) and on a LPS-stimulated macrophage (THP1) cell lines respectively, in comparison with agitated/diluted water and scramble DNA sequences prepared in the same conditions (negative controls). For B95-8 proliferative model, high mobility group box 1 protein (HMGB1) was used as reference. Analyzed biological parameters on B95-8 were i) cell proliferation measured after 24 and 48h of incubation with HD SNA and ii) expression of the EBV ZEBRA protein in response to TGF-β by Western-blotting (T+24h). For THP1 model, TNF-α synthesis and release were determined by RT-qPCR and ELISA (protein), after stimulation by LPS (1µg/ml) and HD SNA co-administration.

Results: we demonstrated that HD SNA RA significantly down-regulated TNF-α synthesis and release. This biological activity was showed to be specific (no effect of HD scramble SNA) and related to the level of dilution (maximal effect with higher dilutions). Unexpectedly, a biological effect of agitated/diluted water was also detected in both cellular models. For B95-8 model, this effect resulted in a significant decrease of B95-8 proliferation (comparable to the HMGB1 reference) and an inhibition of ZEBRA expression. Similarly, a reproducible stimulation effect of HD water was obtained in the LPS-stimulated THP1 model.

Conclusions: these findings indicate that highly diluted SNA RA can regulate TNF-α synthesis and release by LPS-stimulated THP1 and support the hypothesis that these homeopathic preparations may act in modulating mRNA expression of the targeted genes. This in vitro work underlines the potential effect of agitated water in context of cellular models for testing biological properties of HD.
Keywords: Specific Nucleic Acids (SNA®); Cellular models; Epstein-Barr virus, Tumor Necrosis Factor-α, Rheumatoid arthritis

References: