

Antiviral Pathway Deregulation of Chronic Fatigue Syndrome Induces Nitric Oxide Production in Immune Cells That Precludes a Resolution of the Inflammatory Response

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Abstract:

Chronic fatigue syndrome (CFS) is a poorly defined medical condition diagnosed by exclusion, which, besides severe chronic fatigue as the hallmark symptom, involves inflammatory and immune activation stigma. Although viral infections are not systematically found in CFS patients, the type I interferon antiviral pathway has been repeatedly shown to be activated in peripheral blood mononuclear cells (PBMC) of the most afflicted patients. An abnormal truncated form of ribonuclease L (37-kDa RNase L) is also found in the PBMC of CFS patients and this protein has been proposed as a biological marker for CFS. Recently, the levels of this abnormal protein have been significantly correlated to the extent of inflammatory symptoms displayed by CFS patients. We report here that active double-stranded RNA-dependent kinase (PKR) is expressed and activated in parallel to the presence of the 37-kDa RNase L and to an increase in nitric oxide production by immune cells. However, PKR upregulation results also in a significant increase followed by a decrease in caspase 3 activity for the samples containing the highest levels of 37-kDa RNase L. This caspase 3 downregulation does not result from increased expression of the anti-apoptotic proteins Bcl-2 and Bcl-X_L. These results therefore suggest that chronic inflammation due to excess nitric oxide production plays a role in CFS and that the normal resolution of the inflammatory process by NF-κB activation and apoptotic induction is impaired. These observations draw new directions for the therapeutic approach of CFS. doi:10.1300/J092v13n04_03

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