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Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome.

Vojdani A, Lapp CW.

Immunosciences Laboratory Inc., Beverly Hills, California, USA.
immunsci@ix.netcom.com

Overlapping symptomatologies between Chronic Fatigue Syndrome (CFS) and Chemical Sensitivity have been observed by different investigators. Therefore, it is of great importance to develop biomarker(s) for possible differentiation between viral induced CFS (without sensitivity to chemicals) versus chemically induced CFS. Since interferon induced proteins 2-5A Synthetase and Protein Kinase RNA (PKR) have been implicated in the viral induction of CFS, the objective of this study was to utilize 2-5A and PKR activity for differentiation between CFS induced by either viruses or chemicals. Based on the CDC definition and criteria, twenty CFS patients who were positive for viral genome(s) (mainly HHV6; HTLVII, EBV, and CMV) and did not have any history of exposure to toxic chemicals were included in this study. As a comparison, the second group of patients consisted of twenty individuals from the same geographical area who were negative for viral genomes but had been exposed to methyl tertiary-butyl ether concentration of up to 70 ppb and benzene concentration up to 14 ppb. All patients complained of fatigue and other symptoms overlapping between the two groups. From all 40 patients, blood was drawn, leukocyte extract was prepared and assayed for 2-5A Synthetase and PKR activity. Clinical specimens which were positive for viral genomes showed from 2.2-38.7 fold increase in 2-5A activity and 1.3-13.5 fold increase in PKR activities over the background of the healthy controls. Similarly, the second group (negative for viral genomes, but exposed to chemicals) showed a 1.1-29.2 fold increase for 2-5A Synthetase and a 1.3-11.6 fold increase for PKR when they were compared to healthy subjects. To elucidate mechanisms involved in viral versus chemical induction of 2-5A Synthetase and PKR, MDBK cell lines were cultured either in the presence or absence of HHV6, MTBE, or Benzene, heat shock proteins and interferon-beta. 2-5A and PKR activities were measured in all the above conditions. A clear induction of 2-5A and PKR was observed when MDBK cells were exposed to HHV6, MTBE, and Benzene. This induction was more significant with HSP90, HSP70, and IFN-beta indicating their involvement in the mechanism of action. However, when MDBK cells were incubated either with MTBE + Benzene or HHV6 in the presence or absence of anti IFN-beta or anti-HSP-70, the activities of both 2-5A and PKR in HHV6 infected cells were inhibited by more than 90% due to addition of anti IFN-beta, and only 20% by addition of anti-HSP70. While in MTBE + Benzene exposed cells anti IFN-beta reduced the activity of these enzymes by 40% and anti-HSP70 by more than 90%. This variation in the induction of 2-5A and PKR by anti-HSP70 or IFN-beta indicates involvement of IFN-beta in viral induction 2-5A and PKR, and HSP involvement in chemical induction of these enzymes.

We conclude that 2-5A and PKR are not only biomarkers for viral induction of CFS, but biomarkers to other stressors that include MTBE and Benzene.

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