

Biochemical evidence for a novel low molecular weight 2-5A-dependent RNase L in chronic fatigue syndrome.

Suhadolnik RJ, Peterson DL, O'Brien K, Cheney PR, Herst CV, Reichenbach NL, Kon N, Horvath SE, Iacono KT, Adelson ME, De Meirleir K, De Becker P, Charubala R, Pfliederer W. (1997)

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Previous studies from this laboratory have demonstrated a statistically significant dysregulation in several key components of the 2',5'-oligoadenylate (2-5A) synthetase/RNase L and PKR antiviral pathways in chronic fatigue syndrome (CFS) (Suhadolnik et al. Clin Infect Dis 18, S96-104, 1994; Suhadolnik et al. In Vivo 8, 599-604, 1994). Two methodologies have been developed to further examine the upregulated RNase L activity in CFS. First, photoaffinity labeling of extracts of peripheral blood mononuclear cells (PBMC) with the azido 2-5A photoaffinity probe, [32P]pApAp(8-azidoA), followed by immunoprecipitation with a polyclonal antibody against recombinant, human 80-kDa RNase L and analysis under denaturing conditions. A subset of individuals with CFS was identified with only one 2-5A binding protein at 37 kDa, whereas in extracts of PBMC from a second subset of CFS PBMC and from healthy controls, photolabeled/immunoreactive 2-5A binding proteins were detected at 80, 42, and 37 kDa. Second, analytic gel permeation HPLC was completed under native conditions. Extracts of healthy control PBMC revealed 2-5A binding and 2-5A-dependent RNase L enzyme activity at 80 and 42 kDa as determined by hydrolysis of poly(U)-3'-[32P]pCp. A subset of CFS PBMC contained 2-5A binding proteins with 2-5A-dependent RNase L enzyme activity at 80, 42, and 30 kDa. However, a second subset of CFS PBMC contained 2-5A binding and 2-5A-dependent RNase L enzyme activity only at 30 kDa. Evidence is provided indicating that the RNase L enzyme dysfunction in CFS is more complex than previously reported.

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