Gene Expression Analysis Identifies Potential Biomarkers of Neurofibromatosis Type 1, Including Adrenomedullin


Plexiform neurofibromas (PNFs) are Schwann cell tumors found in a third of individuals with neurofibromatosis type 1 (NF1). PNFs can undergo transformation to malignant peripheral nerve sheath tumors (MPNSTs). There are no identified serum biomarkers of PNF tumor burden or transformation to MPNSTs. Serum biomarkers would be useful to verify NF1 diagnosis, monitor tumor burden, and/or detect transformation.

We used microarray gene expression analysis to define 92 genes that encode putative secreted proteins in neurofibroma Schwann cells, neurofibromas, and MPNSTs. We validated differential expression by using quantitative reverse transcription polymerase chain reaction (RT-PCR), western blotting, and ELISA assays in cell-conditioned medium and control and NF1 patient sera.

Of 13 candidate genes evaluated, only adrenomedullin (ADM) was confirmed as differentially expressed and elevated in serum of NF1 patients. ADM protein concentration was further elevated in the serum of a small sampling of NF1 patients with MPNSTs. MPNST-cell-conditioned medium, containing ADM and hepatocyte growth factor, stimulated MPNST migration and endothelial cell proliferation.

Thus, microarray analysis identifies potential serum biomarkers for disease, and ADM is a serum biomarker of NF1. ADM serum levels do not seem to correlate with the presence of PNFs, but may be a biomarker of transformation to MPNSTs.

Link: http://www.ncbi.nlm.nih.gov/pubmed/20739432