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Detection of Pancreatitis-Associated Protein for Use in Cystic Fibrosis Screening of Newborns

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Cystic Fibrosis (CF) is a common autosomal recessive disorder that afflicts 1:2000 caucasian births. Screening for this disease has been possible since 1985, but the accuracy of the test has always been questionable. The widely used Immunoreactive Trypsin (IRT) test for CF tends to be unreliable because elevated levels of trypsin occur in many individuals, even those without cystic fibrosis. A new assay to use in conjunction with the trypsin test may enhance the accuracy of CF screening.

Pancreatitis-associated protein (PAP) is a 16 Kd protein present in small amounts in the normal pancreas but is overexpressed during the acute phase of pancreatitis. Mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene can lead to lung, pancreas and sweat gland dysfunction. Since this mutation leads to increased levels of PAP, it can be used to identify individuals affected with CF at birth. To develop an immunoassay for detection of PAP, synthetic peptides corresponding to the C-terminus and N-terminus of human PAP were synthesized, and antibodies against these peptides were raised in rabbits. The C-terminal peptide antibody reacted with full length PAP and can be used for PAP detection. A fusion protein of human PAP and maltose binding protein (MBP) was created and expressed in E. coli. A preliminary competition ELISA was performed using recombinant PAP to generate a standard for future cystic fibrosis assays. In the future we wish to increase the sensitivity of the assay, develop this standard, and perform recovery studies in human serum.