



MEETING ABSTRACT

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PW03-009 – Genetics of PFAPA syndrome

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Introduction

Periodic Fever, Aphthous stomatitis, Pharyngitis and Adenitis (PFAPA) syndrome is an autoinflammatory disorder of childhood and little is known about the underlying etiology. While mutations involving the IL-1 pathway have been identified in other recurrent fever disorders, including TNF-receptor associated periodic syndrome (TRAPS) and cryopyrin-associated periodic syndrome (CAPS), PFAPA syndrome is not traditionally considered to be a hereditary fever disorder.

Objectives

To evaluate pediatric patients with PFAPA for family histories suggestive of immune dysregulation and to correlate inheritability with immune phenotype.

Methods

Patient data and detailed family histories were collected for over 170 children with recurrent fevers including 70 patients with PFAPA to create a prospective cohort over a 4-year period. DNA was isolated from blood or tonsillar tissue from recurrent fever patients, and *NLRP3* and *TNFRSF1A* were sequenced. Quantitative real time PCR was used to evaluate *IL-36* transcripts in tonsils.

Results

Our cohort reflects the diversity of San Diego, without predilection for any specific ethnic background. Family histories revealed 21% of patients have a first degree relative with recurrent fevers and 12% with tonsillitis in childhood, with only 1.4% reporting a history of recurrent infections. We have identified over 30 families with 2-8 affected members. These patients do not possess mutations commonly seen in other autoinflammatory disorders such as CAPS or TRAPS, suggesting that a novel gene may be involved. Upregulation of IL-36

mRNA expression in tonsils identifies the IL-1 family member IL-36 as a candidate gene.

Conclusion

A substantial portion of our families with PFAPA report childhood histories of recurrent fevers that resolved either spontaneously or with tonsillectomy, indicating a possible dominantly inherited trait that impacts the developing immune system, including the tonsils.

Disclosure of interest

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