

RARE LUNG DISEASES

PULMONARY ALVEOLAR PROTEINOSIS:

PULMONARY TRANSPLANTATION OF MACROPHAGE PROGENITORS AS EFFECTIVE AND LONG-LASTING THERAPY FOR HEREDITARY PULMONARY ALVEOLAR PROTEINOSIS (Happle et al. *Sci Transl Med* 2014; 6: 250ra113)

<http://stm.sciencemag.org/content/6/250/250ra113>

Transplanted wild type bone marrow derived macrophages (BMDM) were able to repopulate the lung, replacing dysfunctional *Csf2rb*^{-/-} macrophages with near normal alveolar macrophages. Lung function, CT opacities and BAL protein and sediment all improved 6 months post transplant. Pulmonary macrophage transplant (PMT) also led to significant disease resolution.

Final statement: Pulmonary macrophage transplant was proven to be a potential treatment strategy for hereditary pulmonary alveolar proteinosis.

LANGERHANS CELL HISTIOCYTOSIS

BRAF-V600E EXPRESSION IN PRECURSORS VERSUS DIFFERENTIATED DENDRITIC CELLS DEFINES CLINICALLY DISTINCT LCH RISK GROUPS (*Berres et al, J Exp Med* 2014; 211: 669-683)

<http://jem.rupress.org/content/211/4/669>

In this study genotyping was performed by qPCR of whole lesion genomic DNA. The presence of BRAF V600E mutation was associated with a higher risk of recurrent or refractory LCH. There was almost a two-fold increase in relapse. There was no correlation with age, extent of lesions, clinical risk status, central nervous system involvement or development of diabetes insipidus. There was also no association with “high risk disease” or overall survival.

Final statement: In high-risk LCH, somatic BRAF mutations arise very early, whereas BRAF-V600E mutations in patients with low-risk LCH were not identified in circulating cells.

PRIMARY CELL DYSKINESIA

CLINICAL FEATURES OF CHILDHOOD PRIMARY CILIARY DYSKINESIA BY GENOTYPE AND ULTRASTRUCTURAL PHENOTYPE (*Davis SD et al, Am J Respir Crit Care Med* 2015; 191: 316-324)

http://www.atsjournals.org/doi/abs/10.1164/rccm.201409-1672OC?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed#.VgKrUN9VhBc

This was a registry-based study looking at the correlations between genotype and clinical phenotype of PCD. 118 patients were studied here. Most patients had

neonatal respiratory distress, chronic wet cough, otitis media and chronic nasal congestion. Four groups were identified:

1. Outer Dynein Arms defect (46%) only
2. ODA/Inner dynein Arm (IDA) defect (34%).
3. IDA/Central apparatus (CA)/micro tubular disorganization (MTD) defect (34%).
4. CA or IDA defect (5%).

Group 3 was identified earlier in life but with worse airflow obstruction, more radiographic disease and poorer growth. There was no significant difference in bacterial isolates. The rate of lung function decline in group 3 was comparable to that seen in cystic fibrosis.

Final statement: The benefits of genetic testing in this group of patients may be beneficial in defining prognosis.

LYMPHANGIOMATOSIS

KAPOSIFORM LYMPHANGIOMATOSIS: A DISTINCT AGGRESSIVE LYMPHATIC ANOMALY
(Croteau SE et al. *The Journal of Paediatrics* 2014; 164: 383-388)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3946828/>

A new histopathological diagnosis, Kaposiform Lymphangiomatosis (KLA) was identified in 20 patients at the Boston Children's Vascular Anomalies centre. It is characterised by clusters of kaposiform hemosiderin D2-40, Lyve-1 Pox-1 positive spindled lymphatic endothelial cells. KLA patients presented at an average age of 6.5 with mediastinal/paraspinal masses, pulmonary parenchymal septal and interstitial thickening, problematic chylous and pericardial effusions, dyspnoea, haemoptysis and blood abnormalities (i.e. Elevated D-dimer and fibrin split products, low platelets and low fibrinogen). The five year survival was 51% with an overall survival of 34% which is much lower than generalized lymphatic abnormalities.

Final statement: KLA is a new subtype of generalized lymphatic anomalies.