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HCD. Histiocytic Disorders

NIHR BioResource – Rare Diseases study project

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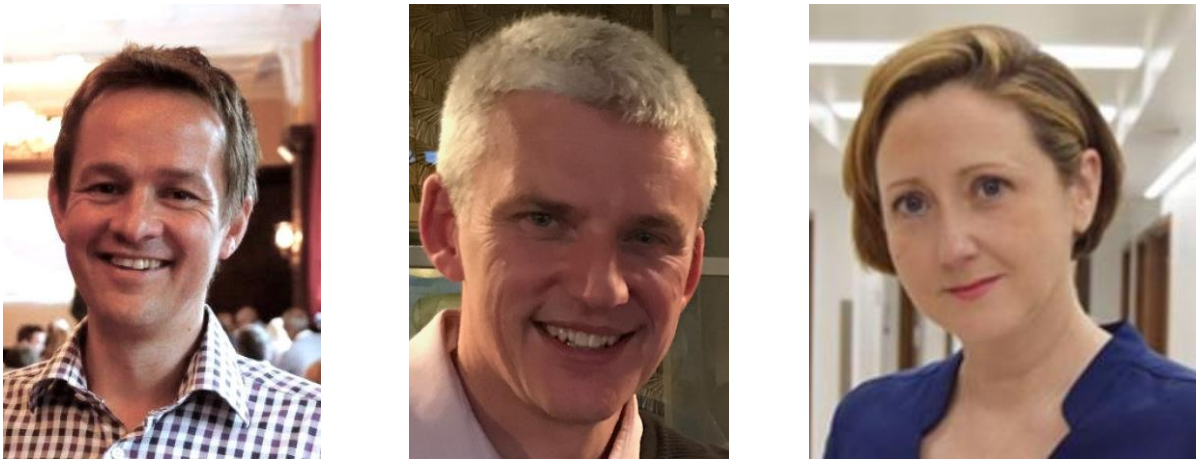

(L-R) Prof. Matthew Collin, Dr Johannes Viser, Dr Claire Booth; HCD project Leads

Summary

Histiocytic Disorders are characterised by excessive accumulation or activation of tissue-resident white blood cells known as ‘histiocytes’. Histiocytes are present in nearly all tissues and ultimately come from the bone marrow or blood-forming organs. In health they perform critical functions maintaining the health of tissues. In a histiocytic disorder, accumulation of activated histiocytes can have severe consequences leading to tissue damage and organ failure.

Two major types of histiocytosis are known. The first type includes diseases such as Langerhans Cell Histiocytosis (LCH), Juvenile Xanthogranuloma (JXG), Erdheim Chester Disease (ECD), and Rosai Dorfman Disease (RDD). In these conditions, histiocytes are abnormally programmed by genetic mutations, causing them to accumulate and attract other immune cells to form inflammatory masses, destructive lesions or fibrous scar tissue.

The second type of histiocytic disorder is known as Haemophagocytic Lympho-Histiocytosis (HLH). HLH is characterised by the presence of super-activated histiocytes that cause body-wide inflammation and prevent the production of blood cells by the bone marrow. In children HLH usually only occurs when there is an inherited genetic defect, often in the genes required to make immune responses to viruses. In adults, HLH can be triggered by infections or cancer and the role of genetic factors is less well understood.

In addition to these two main types, there are many rare and poorly characterised disorders in which histiocytosis is observed. These may also have a genetic cause that is no yet known.

The NIHR BioResource will enable much more rapid progress in understanding the genetic basis, prevalence and health impact of Histiocytic Disorders. This is vital for making rapid and accurate diagnosis, using personalised medicine approaches, and defining the healthcare resources required to care for patients effectively.

Recruitment Criteria

Inclusion

1) Neoplastic Histiocytosis

Children or adults with a diagnosis of histiocytosis including Langerhans Cell Histiocytosis (LCH), Juvenile Xanthogranuloma (JXG), Erdheim Chester Disease (ECD), Rosai Dorfman Disease (RDD) and any other histiocytic disorder of groups L, C, R and M, as defined by Emile et al. 2016[1].

2) Haemophagocytic Lympho-Histiocytosis

a) Children meeting the diagnostic criteria for HLH according to Histiocyte Society guidelines described by Henter et al. 2007[2] based upon the presence of 5/8 of:
   - fever
   - splenomegaly
   - cytopenias
   - hypertriglyceridaemia or hypo-fibrinogenaemia
   - haemophagocytosis
   - hyperferritinaemia
   - elevated soluble CD25
   - absent NK activity

b) Adults meeting the diagnostic criteria for HLH according to Histiocyte Society guidelines (above) or alternatively, exceeding an H Score of 169 as defined by Fardet et al. 2014[3] based upon weighted scores of:

Parameter	degree	H	degree	H	degree	H
Immunosuppressed	no	0	yes	18		
Temperature (°C)	<38.4	0	38.4-39.4	33	>39.4	49
Organomegaly	No	0	hep or spleen	23	both	38
No. of cytopenias	1 lineage	0	2 lineages	24	3 lineages	34
Ferritin (ng/ml)	<2000	0	2000-6000	35	>6000	50
Triglyceride (mmoles/L)	<1.5	0	1.5-4.0	44	>4	64
Fibrinogen (g/L)	>2.5	0	≤2.5	30		
AST (IU/L)	<30	0	≥30	19		
Hemophagocytosis	no	0	yes	35		

3) Rare, poorly characterised disorders with histiocytic pathology

Including but not limited to:

- Orofacial granulomatosis
- Giant cell granuloma
- Blau's syndrome
- Granulomatous angiitis
- Granuloma annnulare
- Actinic granuloma
- Granulomatous Rosacea

References

1. Emile JF et al. 2016. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016 Jun 2;127(22):2672-81. Pubmed ID 26966089. https://www.ncbi.nlm.nih.gov/pubmed/26966089
2. Henter JI et al 2007. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007 Feb;48(2):124-31. Pubmed ID 16937360. https://www.ncbi.nlm.nih.gov/pubmed/16937360
3. Fardet L et al. 2014. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol. 2014 Sep;66(9):2613-20. Pubmed ID 24782338. https://www.ncbi.nlm.nih.gov/pubmed/24782338