Understanding dendritic cell lineages in Erdheim-Chester disease: towards a non-invasive diagnosis

(ECD-GA Grant Recipient; Grant to run Sept. 2012- Sept. 2013)

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Abstract:

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis first described by Jakob Erdheim and William Chester in 1930. By December 2011, more than 450 distinct cases have been reported in the medical literature. ECD is truly a systemic and heterogeneous disease mainly involving the bones, lungs, skin, retro-orbital tissues, central nervous system (CNS), pituitary gland, large vessels, kidneys, retroperitoneum, and heart. The clinical course of ECD is largely dependent on the extent and distribution of the disease, which may range from asymptomatic bone lesions to multisystemic, life-threatening forms with poor prognosis, especially in case of specific CNS or cardiovascular involvements. ECD diagnosis is currently based on clinical, radiologic, and typical pathologic features with the biopsy specimen displaying infiltration by $CD68^{+}CD1a^{-}$ foamy histiocytes, which emphasizes the distinction from Langerhans cell histiocytosis. Importantly, histiocytoses are a group of rare and heterogeneous disorders characterized by the accumulation and/or proliferation of histiocytes within the affected tissues. The generic term "histiocytes" refers to several types of cells comprised within the macrophage and dendritic cell lineages. These cells are believed to arise from the CD34+ stem cell in the bone marrow, and to further differentiate either into CD14+ or CD14- cells. CD14+ cells include the circulating monocytes that differentiate into tissue histiocytes (macrophages & interstitial dendritic cells). Conversely, CD14- cells either differentiate into Langerhans cells or CD123+ plasmacytoid dendritic cells [1, 2]. During this research, we will compare both the phenotype and functionality of the different circulating dendritic cell subsets between a large cohort of patients with ECD and an identical number of sex- and age-matched controls. By systematically assessing both the phenotype and functionality of the different dendritic cell lineages involved in the pathogenesis of ECD, **the aim of our project is to understand the primary mechanisms involved in the pathogenic differentiation of histiocytes in ECD, as well as to use these data to derive a screening & diagnostic test for ECD that would rely on blood sampling without the need for a biopsy.**

Keywords: Erdheim-Chester disease, Dendritic cells, histiocytes, phenotype, functionality, diagnosis test.