THE GRADUATE COLLEGE OF THE UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

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FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
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Department of Pathology

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Minor salivary gland damage and T cell involvement in Sjögren's *Syndrome*

COMMITTEE IN CHARGE: A. Darise Farris, Ph.D, Chair, Mary Beth Humphrey, M.D., Ph.D., Yuechueng Liu, Ph.D., Kathy L. Sivils, Ph.D., Joe Zhao, Ph. D.

ABSTRACT: Sjögren's syndrome is a systemic rheumatic disease with organ-specific manifestations. Patients with SS, predominantly women over 40, experience chronic dry, gritty eye and severe dry mouth. The target organs of SS are the lacrimal and salivary glands. These glands show characteristic infiltration by lymphocytic cells, predominantly CD4+ T cells, as well as fibrosis and fatty replacement of the functional tissue. Historically, fibrosis in the salivary gland has been widely observed but ascribed to age rather the pathology of Sjögren's Syndrome. Using a precise method of quantification, we determined that fibrosis is significantly increased in SS as compared to sicca patients, and is a fundamental form of SS pathology closely associated with focal lymphocytic infiltration. Fatty infiltration of exocrine tissue is a well-characterized reaction to trauma and/or ageing, so we assessed whether the extent of fatty replacement in SS SG tissue was part of SS pathology. We determined that fatty replacement was equally represented in SS and sicca patients, and associated only with patient age. CD4+ T cells predominate in salivary gland (SG) inflammatory lesions in Sjögren's syndrome (SS). Via a single-cell approach, we retrieved paired T cell receptor sequences from patient SG and peripheral blood and determined that T cells in the SG are clonally expanded (a feature absent in peripheral blood) and share sequence characteristics suggesting antigen driven proliferation. Increased clonal expansion associates significantly with loss of salivary function and increased SG fibrosis