

COMPARATIVE LYMPHATIC, OCULAR, AND METABOLIC PHENOTYPES OF FOXC2 HAPLOINSUFFICIENT AND AP2-FOXC2 TRANSGENIC MICE**A. Noon, R.J. Hunter, M.H. Witte, B. Kriederman, M. Bernas, M. Rennels, D. Percy, S. Enerbäck, R.P. Erickson**

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ABSTRACT

FOXC2 mutations cause the lymphatic/ocular disorder Lymphedema-Distichiasis (LD), and Foxc2 haploinsufficient mice mimic this disorder. To determine if FOXC2 overexpression might also cause lymphatic and/or ocular abnormalities, we performed dynamic lymphatic imaging (Evans blue dye), ocular tissue examination, and metabolic profiles in mice: transgenic for FOXC2 with an adipocyte (aP2) promoter (aP2-FOXC2 Tg), heterozygous for targeted disruption of Foxc2 (Foxc2^{+/-}), or compound heterozygous and transgenic (Foxc2^{+/-}, Tg) compared to wild-type controls (WT). Foxc2^{+/-}; aP2-FOXC2 Tg; and Foxc2^{+/-}, Tg, exhibited LD's distinctive hyperplastic lymphatic phenotype characterized by increased number of lymphatic channels and lymph nodes as well as retrograde lymph reflux. Foxc2^{+/-}, and Foxc2^{+/-}, Tg but not aP2-FOXC2 Tg or WT showed an abnormal ocular phenotype. Previously described alterations in brown/white fat distribution and lean phenotype in aP2-FOXC2 transgenics were confirmed. AP2-FOXC2 Tg immunohistochemistry disclosed aberrant FOXC2 expression in ectopic sites, especially embryonic heart. Lymphatic system links with fat metabolism are discussed.