

78. MACROPHAGE MIGRATION AND LUTEAL REGRESSION IN OVARIES OF LEUKOCYTE ADHESION MOLECULE-DEFICIENT (ICAM-1^{-/-}) MICE

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Luteal regression is an ovarian remodeling event involving apoptosis of luteal cells, an influx of macrophages thought to phagocytose luteal cell debris, and resorption of the corpus luteum (CL). Macrophage adhesion and migration in many tissues is mediated by ICAM-1 (a cellular adhesion molecule which acts as a counter-receptor for leukocyte β 2-integrins); and increased ICAM-1 expression has been associated with macrophage infiltration in regressing CL of the rat. To test whether ICAM-1 mediates macrophage infiltration during regression, CL of ICAM-1 null (ICAM-1^{-/-}) mice were analysed by immunohistochemistry for markers of macrophages (F4/80) and luteal cell apoptosis (caspase-3). Ovaries of adult cycling ICAM-1^{-/-} females showed abundant macrophages in regressing CL indicating that ICAM-1 is not required for macrophage migration during luteolysis. In older mice (6 months of age), wildtype (WT) ovaries consisted primarily of follicles and CL, however, ICAM-1^{-/-} ovaries consisted almost entirely of stroma with only a few follicles and CL. These "stromal" cells were reminiscent of luteal cells (hypertrophied and eosinophilic) suggesting that CL regression failed to resolve normally resulting in accumulation with time. To test this, WT and ICAM-1^{-/-} mice were hormonally primed to stimulate luteinization and subsequent regression, with PMSG/ hCG for 4 or 6 days, and the regressing CL were compared. Preliminary results showed that the CL of ICAM-1^{-/-} mice are less regressed than WT at 4 d post-hCG, an effect which is most pronounced at 6 d post-hCG. Immunohistochemical staining patterns for F4/80 and caspase-3 were similar in WT and ICAM-1^{-/-} ovaries indicating that macrophages are present and luteal cell apoptosis is occurring in the "regressing" CL. Concurrently, to test whether the lack of ICAM-1 and a potential defect in luteal regression would impact fertility, female ICAM-1^{-/-} and WT littermates were housed with WT males. After 6 months ICAM-1^{-/-} females had produced normal numbers of litters and pups. Thus, ICAM-1 is not essential for female fertility. That CL regression was delayed despite the presence of luteal macrophages in ICAM-1^{-/-} ovaries indicates that during luteal regression ICAM-1 is likely to be more important for macrophage activation and/or phagocytosis than recruitment or migration.