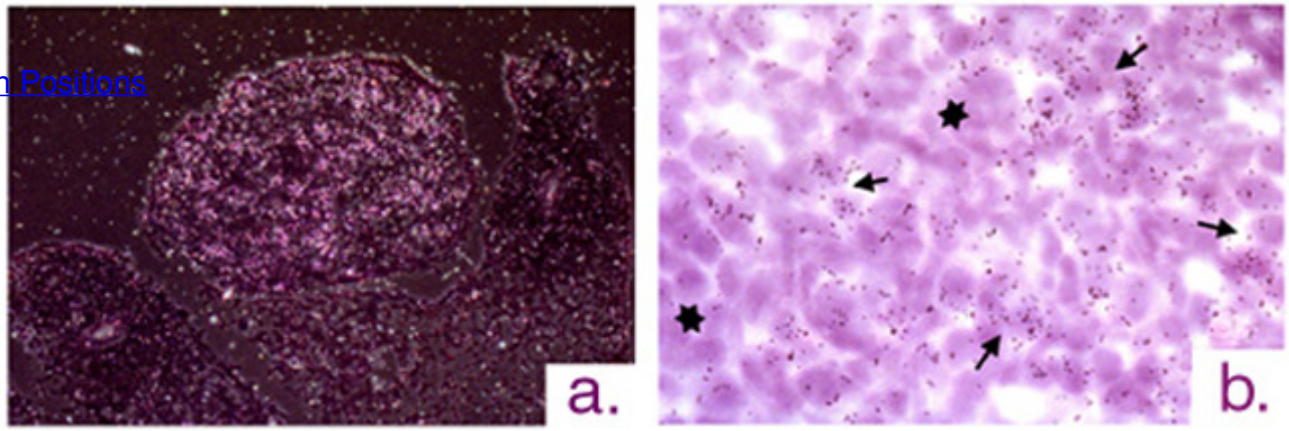
Germline Recombination in the Mouse

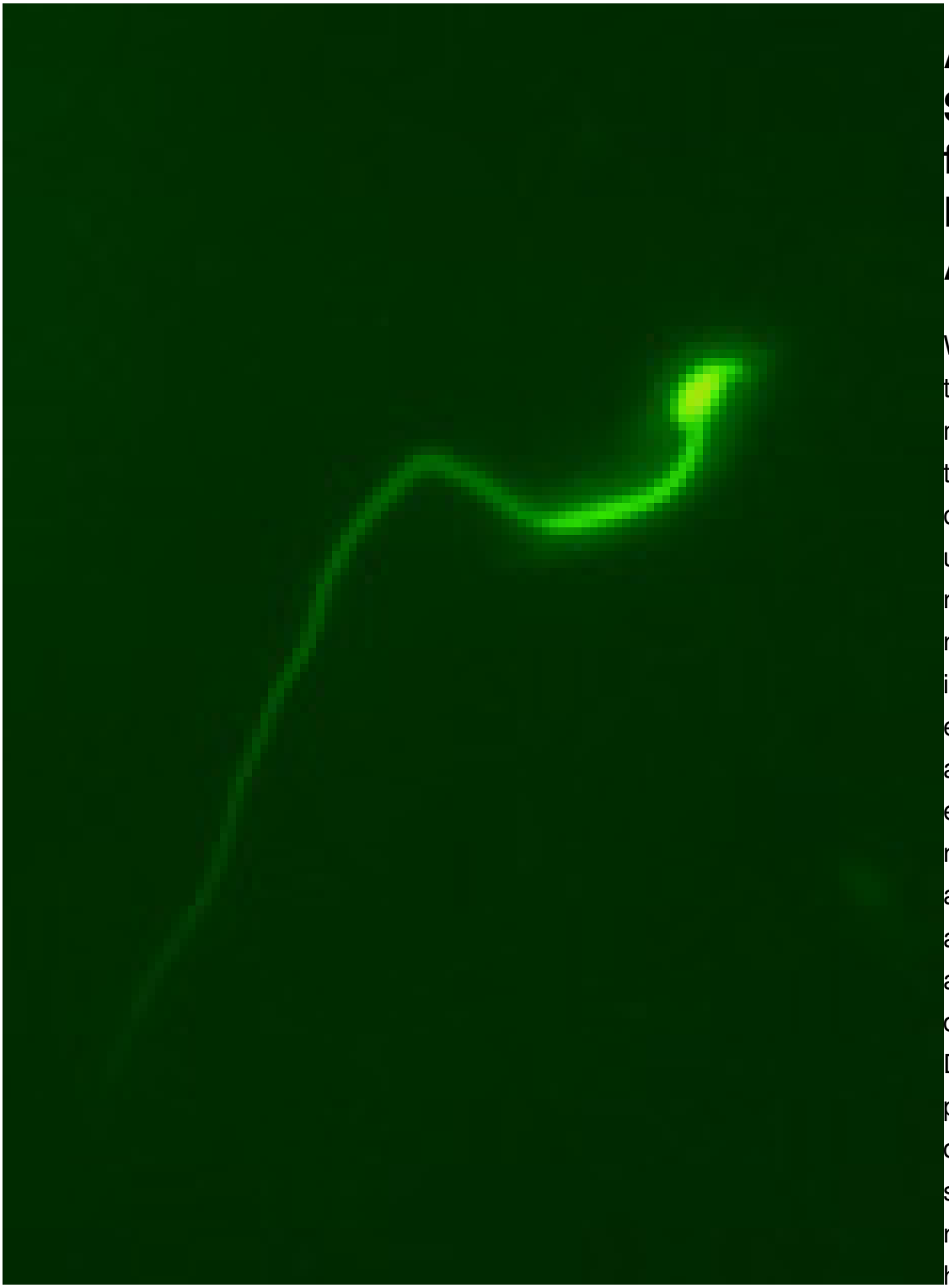
Spo11 and the Initiation of Meiotic Recombination



In females, meiosis is initiated during fetal development. Digital micrographs of fetal ovary at embryonic day 14.5 hybridized to the antisense Spo11 probe are shown here in panels a and b. — Dark field (panel a, magnification 20X) and bright field (panel b, magnification 100X) images appear above. In panel b, arrows indicate clusters of labeled oocytes that correspond to the patchy areas of autoradiographic grains in panel a, and stars indicate clusters of oocytes devoid of hybridization signal.

Unlike its DNA repair role in somatic cells, homologous recombination has a distinct role in meiosis in ensuring proper chromosome segregation. In yeast, an early step of the meiotic program is the introduction of double-strand breaks into chromosomes by the Spo11 protein to promote recombination between homologs. It is not clear when meiotic recombination is initiated in mammals, but it has been speculated to occur later in meiosis, after chromosomes have already synapsed. Dr. Scott Keeney's laboratory in the Molecular Biology Program and this laboratory have collaborated to clone the mouse Spo11 gene in order to resolve the timing question and other issues regarding meiotic recombination in the mouse (Keeney et

al. Genomics. 1999). Expression of the Spo11 gene, carried out with Katia Manova of the Molecular Cytology Core Facility, is consistent with a role early in meiosis. A mouse knockout of Spo11 is currently underway in the lab by Frédéric Baudat in collaboration with the Keeney lab.



Fluorescent mouse sperm, after staining with a fluorescein- ß-galactoside conjugate.

A Fluorescence Sperm Assay for Germline Recombination Analysis

We expect the analysis of the role of Spo11 in meiosis to add tremendously to our ongoing efforts aimed at understanding recombination and the role of DNA repair genes in the animal. These efforts include the analysis of recombination events within lacZ reporter substrates, using a sperm fluorescence assay. With this approach, we have determined that unusual DNA structures (i.e., palindromes, as well as double-strand breaks) stimulate germline recombination events to a high degree (Akgün et al. Mol Cell Biol. Romanienko PJ, Baudat F, Jasin M. In Preparation.).

Moynahan ME, Akgun E, Jasin M. 1996 A model for testing recombinogenic sequences in the mouse germline. Hum Mol Genet. 1996;5:875-886.

Akgun E, Zahn J, Baumes S, Brown G, Liang F, Romanienko PJ, Lewis S, Jasin M. 1997 Palindrome resolution and recombination in the mammalian germline. Mol Cell Biol. 1997;17:5559-5570.

Keeney S, Baudat F, Angeles M, Zhou ZH, Copeland NG, Jenkins NA, Manova K, Jasin M. 1999 A mouse homolog of the S. cerevisiae meiotic recombination DNA transesterase Spo11p. Genomics 1999;61:170-182.