

26. Linkage analysis

1 unit, Scott Keeney October 6, 2025

I. Introduction to linkage analysis

Overview of meiosis and recombination

Discovery of sex linkage

Constructing genetic maps based on recombination frequency

Relationship between genetic maps and physical maps

II. Tetrad analysis

Linkage analysis when all of the products of a single meiosis can be recovered

Tetrad segregation patterns

Assigned Paper:

(Please read, but we will not discuss in class except briefly; for purposes of this lecture, the first four pages of the paper are relevant)

Jain D, Puno MR, Meydan C, Lailier N, Mason CE, Lima CD, Anderson KV, and Keeney S (2018) ketu mutant mice uncover an essential meiotic function for the ancient RNA helicase YTHDC2. eLife doi: 10.7554/eLife.30919. PMC5832417

Additional reading:

Li Y, Klena NT et al. (2015) Global genetic analysis in mice unveils central role for cilia in congenital heart disease. Nature 521(7553):520-4. PMID: 25807483

Ott J, Wang J, Leal SM (2015) Genetic linkage analysis in the age of whole-genome sequencing. Nature Rev Genet. 16: 275-84

Perkins, D.D. (1949) Biochemical mutants in the smut fungus Ustilago maydis. Genetics 34: 607-626.

Bowcock AM, Anderson LA, Friedman LS, Black DM, Osborne-Lawrence S, Rowell SE, Hall JM, Solomon E, King MC. THRA1 and D17S183 flank an interval of < 4 cM for the breast-ovarian cancer gene (BRCA1) on chromosome 17q21. Am. J. Hum Genet. 52, 718-22 (1993).

Ellis NA, Groden J, Ye TZ, Straughen J, Lennon DJ, Ciocchi S, Proytcheva M, German J. (1995) The Bloom's syndrome gene product is homologous to RecQ helicases. Cell. 83:655-666.

Fishel R, Lescoe MK, Rao MR, Copeland NG, Jenkins NA, Garber J, Kane M, Kolodner R. The human mutator gene homolog MSH2 and its association with hereditary nonpolyposis colon cancer. Cell. 75, 1027-1038 (1993).

Kauppi L, Jeffreys AJ, and Keeney S (2004) Where the crossovers are: Recombination distributions in mammals. Nature Rev. Genet. 5, 413-424.

Liem KF Jr, He M, Ocbina PJ, Anderson KV. (2009) Mouse Kif7/Costal2 is a cilia-associated protein that regulates Sonic hedgehog signaling. Proc Natl Acad Sci U S A. 106:13377-82.

Thacker D, Lam I, Knopp M, and Keeney S (2011) Exploiting spore-autonomous fluorescent protein expression to quantify meiotic chromosome behaviors in Saccharomyces cerevisiae. Genetics 189, 423-439.