

30. Genetic Drivers of Hematopoietic Malignancies

1 unit, Ross Levine, April 1, 2026

1. Genetic Basis of Human Cancers
 - a. Discovery of Oncogenes
 - b. Two hit Knudson model and tumor suppressor genes
2. Lessons from large scale genomic studies
 - a. Lessons thus far
 - b. Identification of recurrent disease alleles
3. Validation of cancer “drivers”
 - a. Computational approaches
 - b. Functional validation
 - c. Integration with shRNA screens and CN data
4. Preclinical Cancer Models
 - a. In vitro vs. in vivo approaches
 - b. Genetically engineered murine models
 - c. PDX Models
5. Biologic and Translational Insights
 - a. Mechanisms of transformation
 - b. Preclinical therapeutic studies

Discussion Paper:

Sango J, Carcamo S, Sirenko M, Maiti A, Mansour H, Ulukaya G, Tomalin LE, Cruz-Rodriguez N, Wang T, Olszewska M, Olivier E, Jaud M, Nadorp B, Kroger B, Hu F, Silverman L, Chung SS, Wagenblast E, Chaligne R, Eisfeld AK, Demircioglu D, Landau DA, Lito P, Papaemmanuil E, DiNardo CD, Hasson D, Konopleva M, Papapetrou EP. RAS-mutant leukaemia stem cells drive clinical resistance to venetoclax. *Nature*. 2024 Dec;636(8041):241-250. doi: 10.1038/s41586-024-08137-x. Epub 2024 Oct 30. PMID: 39478230; PMCID: PMC11618090.

Background: Cancer Genome Landscapes Bert Vogelstein, Nickolas Papadopoulos, Victor E. Velculescu, Shibin Zhou, Luis A. Diaz Jr., and Kenneth W. Kinzler *Science* 29 March 2013: 1546-1558.