In Vitro Selection for Isoantigenic Variants of Mammalian Somatic Cells. HOWARD M. CANN * and LEONARD A. HERZENBERG,* Stanford University School of Medicine. Introduced by Norman Kretchmer.

Genetic analysis of mammalian somatic cells will be facilitated with a method for rapid screening of large numbers of individual cells to detect rare variants. Applying the techniques of microbial genetics to cell culture, particularly selection of variants by providing an environment in which type strain cells are suppressed or killed while the variant sought is unaffected, one can develop a set of markers which can then, hopefully, be used for genetic analysis. Variation at the H-2 chromosomal locus, a complex locus of the mouse which determines a number of isoantigens on the cell membrane, affords a system for developing in vitro selective markers.

In this laboratory we have developed a method for selecting isoantigenic variants of cultured mouse lymphoma cells with anti-H-2 isoantiserum and complement. After incubation of an H-2^d lymphoma, growing in continuous culture, with complement and isoantibodies to the antigenic components specified by the H-2^d allele, 95%-99% of cells are killed, as measured by ability to form clones. Cell killing begins as soon as the components of the system are mixed with the cells, and no further killing occurs after 5-10 minutes at 37 C.

Selection of isoantigenic variants should be most feasible with a cell line heterozygous at the H-2 locus. Change in one allele could then be detected by immunoselection. Nevertheless, in an effort to select isoantigenic variants, 8 clones were randomly picked from a lymphoma cell population (originally H-2^d) surviving 14 selective cycles; each cycle consisted of exposure to anti-H-2^d isoantibody and complement and regrowth of survivors

* By invitation.