

# Researchers Uncover Evidence of Early Genomic Aberrations in Uveal Melanoma

Researchers from Sylvester Comprehensive Cancer Center and Bascom Palmer Eye Institute at the University of Miami Miller School of Medicine have uncovered evidence that genomic aberrations in uveal melanoma that lead to metastasis may occur far earlier in tumor evolution than previously believed.



“Uveal melanoma is the most deadly eye disease in adults,” said J. William Harbour, M.D., associate director for basic research at Sylvester and vice chairman for translational research at Bascom Palmer, whose laboratory conducted the study

published online January 9 by the journal *Nature Communications*. “It is defined by key genetic events, several of which we originally discovered, that lead to metastasis. Using the Pegasus High Performance Computing Facility at the University of Miami’s Center for Computational Science, we were able to show that these genetic events occur early and close together in molecular time. This implies that the metastatic proclivity of uveal melanoma is set in stone early in tumor evolution and may explain why advances in primary treatment have not improved survival.”

The findings fundamentally change our thinking about how this

eye cancer progresses, said Harbour. It was previously thought that the genomic aberrations and associated metastatic risk accumulated slowly over time, but he and his research colleagues found that these aberrations appear to arise abruptly, around the same time. Harbour said this has profound implications for understanding why advances in primary treatment have not improved survival, and suggests that earlier treatment of a subset of high-risk small tumors with dangerous genomic aberrations may be necessary to improve outcomes.

“This study is by far the largest to date analyzing uveal melanoma samples by next-generation sequencing, and the first to use sophisticated clonality bioinformatic techniques to elucidate genomic evolution in this cancer,” said Harbour.

The journal [article](#) describing the research findings, “Punctuated evolution of canonical genomic aberrations in uveal melanoma,” was co-authored by several medical and graduate students working in Harbour’s laboratory – M.D. students Michael A. Durante and Louis Z. Cai, Christina L. Decatur, M.D., Stefan Kurtenbach, Ph.D., and Matthew G. Field, M.S. – in collaboration with two researchers at the National Heart and Lung Institute at Imperial College London.

The next step, said Harbour, will be a five-year, 30-center NCI-sponsored clinical trial – the Collaborative Ocular Oncology Group Study No. 2 (COOG2) – to identify early biomarkers for uveal melanoma metastasis. The trial will examine how best to use targeted ultra-deep next-generation sequencing for these key genomic aberrations in the care of patients.