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Boris C. Bastian, MD, PhD, senior author of the study and Chair of the  
Department of Pathology at Memorial Sloan Kettering Cancer Center

"These findings are significant because we now have a much better understanding of the precise mechanism of this disease, which may yield targets and treatments in the future," said Boris C. Bastian, MD, PhD, Chair of the Department of Pathology at Memorial Sloan Kettering Cancer Center and senior author of the study. "Currently, once this type of melanoma has spread beyond the eye, therapeutic options are extremely limited," added Dr. Bastian.

The eye is the second most common site in the body for melanomas, after the skin. There are about 1,500 people diagnosed with melanoma of the eye in the US each year. Most frequently, melanomas of the eye occur in the part of the eye known as the uveal tract — the vascular layer that includes the iris (the pigmented cells surrounding the pupil), the ciliary body (the ring-shaped muscle that changes the size of the pupil and the shape of the lens when the eye focuses), and the choroid (the pigmented layer under the retina). Most patients with melanoma of the eye experience no symptoms until the tumor has become large enough to cause vision problems. In this study, DNA was extracted from tumor samples of patients and genetic sequencing was performed. To validate this new oncogene, immunocompromised mice were injected with cells engineered to harbor the mutated genes and monitored for the formation of tumors.

Previous studies from this group have revealed another oncogene associated with uveal melanoma, called *GNAQ*. Prior to the discovery of *GNAQ* and *GNA11*, genetic mutations responsible for uveal melanoma were completely unknown. Based on this latest research and recent studies, 83 percent of uveal melanomas are now known to have an active mutation in the *GNAQ* or *GNA11* oncogenes.

In addition, said Dr. Bastian, "since the large majority of uveal melanomas harbor mutations in these two oncogenes, this suggests that the activation of the Gq/11 pathway is the main route to the development of uveal melanoma and identifies a brand new target for therapeutic intervention."

Researchers from the University of British Columbia, the University of California, San Francisco and the Medical University of Graz, in Austria collaborated on this work. Financial support was provided by the NIH, the Melanoma Research Alliance, the Canadian Institutes of Health, the Canadian Cancer Society, the European Commission, and the Jubilaeumsfonds of the Oesterreichische Nationalbank.

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