CCAH Update
UCDAVIS VETERINARY MEDICINE

Genetics Unravel Clues to Gliomas

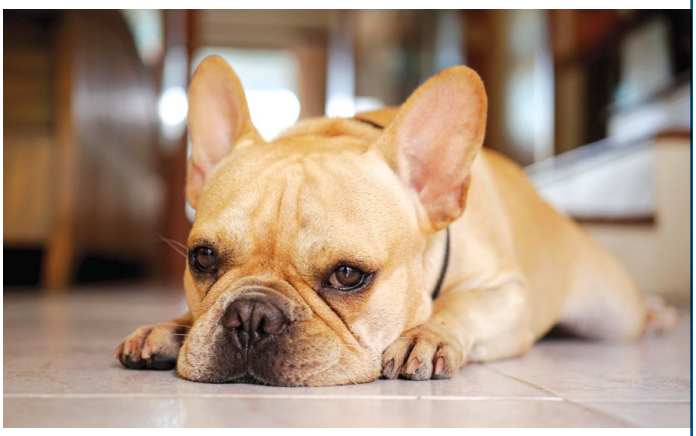
Sometimes a trip to the water cooler delivers more than a refreshing drink—it can also lead to productive research collaborations that shed light on topics of critical concern to animals and humans. Dr. Danika Bannasch, the Maxine Adler Endowed Chair in Genetics, recalls numerous impromptu discussions in the hallways of the Center for Companion Animal Health (CCAH) with Dr. Peter Dickinson, a veterinary neurologist. For decades, he'd been puzzled by why he saw a higher incidence of gliomas among specific dog breeds, particularly in brachycephalic canines such as boxers, bulldogs and Boston terriers.

"What is it about brachycephaly and gliomas?" Bannasch recalls him asking her. "You're the geneticist—why don't you find out!"

Bannasch and Dickinson joined a team with two Swedish scientists that used genome mapping across 25 dog breeds to identify three candidate genes associated with glioma development in canines. The study, published in *PLoS Genetics*, may provide insights into how these often untreatable brain tumors form in dogs and possibly in humans.

A second breakthrough concerning gliomas in dogs came a few months later and provided further definition of the candidate genes while suggesting a common pathway in dogs and humans. The research team, led by Dickinson, also included Drs. Dan York, Robert Higgins, Richard LeCouteur, Bannasch and researcher Nikhil Joshi. Results appeared in the *Journal of Neuropathology & Experimental Neurology*. The study was supported by donors to the CCAH, UC Davis, The Paul and Borghild T. Petersen Foundation and the Maxine Adler Endowment.

"Cancer is cancer," says Dickinson, who has spent the past 17 years researching gliomas in dogs and pursuing a canine model to develop translational therapies in humans. "The big pathways altered in humans are likely to be altered in dogs as well. The details may vary but it's likely to be the same big picture overall, so it's smart to use dogs as a model to identify potential genes for gliomas in humans."



Because spontaneous gliomas are the most common form of malignant primary brain tumors in humans and occur at a similar frequency in canines, human neurooncologists have been interested in the association of gliomas in dogs and humans for a long time. Until recently, they didn't have the tools to answer the questions of whether there were particular genes associated with the tumors in both species.

"Now we have the tools for meaningful clinical translation," Dickinson says. "With advanced imaging and treatment equipment in a veterinary hospital setting, we can almost recapitulate what doctors do for humans in dogs."

He is particularly interested in one of the three candidate genes identified, P2RX7, which is involved in immunity in the brain and may be a target for future therapeutic action.

"We've shown association, now we need to prove causation," Dickinson said. "Can we show that the genes we've identified are really responsible for the increased incidence of tumor formation in specific dog breeds?"