FINAL REPORT

Measuring Chemotherapy Drug Resistance in Dogs with T-cell Lymphoma

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RESULTS: New Technology Helps Detect Small Amounts of Drug-Resistant Cancer Cells in Dogs with T-cell Lymphoma
Morris Animal Foundation-funded researchers from North Carolina State University used state-of-the-art DNA technology to help detect small amounts of drug-resistant cancer cells that persist after treatment in dogs with T-cell lymphoma (minimal residual disease, MRD). Accurately monitoring MRD could provide a fuller picture of the effectiveness of different drugs and improve treatment success, quality of life and survival for these patients.

While many dogs achieve clinical remission or appear cancer-free with intensive chemotherapy, low numbers of cancer cells can still linger. These cells are thought to be the cause of eventual treatment failure. Knowing how residual cancer cells levels go up and down after treatment may provide valuable insight on the loss of responsiveness to individual drugs in multi-agent treatments over time.

To find and measure MRD in dogs with T-cell lymphoma, the team used DNA technology to pick out the cells' unique genetic fingerprints among the larger background population of normal cells circulating in the blood. The team followed eight canine patients receiving standard-of-care chemotherapy and successfully isolated white blood cells from blood draws at periodic intervals during treatment. They then harvested and decoded the genetic information and analyzed the data to find out how many copies of the cancer cell fingerprint, if any, were present in the sea of millions of different fingerprints. They found the process could readily measure minute cancer burdens in the blood at all time points sampled.

Findings from this study are an important first step toward further development of DNA technology to monitor residual cancer cells after treatment. This new information could help reduce the number of drugs that are clearly ineffective for a particular patient, providing a more tailored treatment strategy. This conclusion is supported by another finding in the study; researchers noted drugs in the standard-of-care protocol were only superficially effective in their study dogs.

A general view before this study was that most patients induced with chemotherapy that achieved a complete clinical remission also attained a complete molecular remission (i.e., MRD fell below the limit of detection). This view would predict that cells became resistant sequentially over time as each drug was administered. By early detection of this change through next-generation sequencing, it was thought that MRD-guided drug substitutions could lead to repeated reacquisition of molecular remission, thereby prolonging overall survival. However, data from this study suggests that no particular combination of standard chemotherapeutic drugs, at this intensity, will lead to this end. Rather, only intensification (i.e., higher doses with stem cell support) or the addition of some other therapy (alternate drugs; radiotherapy; immunotherapy) will be sufficient to eradicate MRD and improve outcomes for dogs with T-cell lymphoma and perhaps other aggressive cancers.

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