

Rare, But Not Forgotten

Cancer is not a rare disease. In the United States, more than one in three individuals will be diagnosed with cancer over a lifetime. Advances in treatments—even cures—come from studying both the commonalities within patient populations and from our recognition of the molecular differences among cancers that seem similar upon initial observation. As we learn in “RAS Takes Center Stage,” detailed basic research is required to understand and successfully treat even the most common cancer mutations. However, clinicians are beginning to successfully stratify and treat many common cancers, e.g. breast, lung, and skin cancers, based on the molecules that they express.

The same principle holds true for the less common cancers, but sheer paucity in numbers make it difficult for researchers to uncover the molecular principles that govern them. The NIH Clinical Center specializes in studying and treating rare diseases—cancers among them—because of our unique capabilities to bring in and treat a critical mass of patients with cancers that might otherwise be seen only sporadically in more regional facilities. In this issue of *CCR connections*, we highlight several examples of how this capacity is paying off for understudied cancers.

In “Dramatic Responses in a Rare Type of Sarcoma,” Shivaani Kummar, M.D., and her colleagues in CCR and NCI have seen highly encouraging results in the treatment of alveolar soft part sarcoma, which is often misdiagnosed and treated

(unsuccessfully) as a more common sarcoma. Based on the results they observed with cediranib, an inhibitor of vascular endothelial growth factor receptors (VEGFRs), in only 46 patients, a multicenter open-label phase 2 trial is testing the drug in a much larger patient population.

Diffuse large B-cell lymphoma (DLBCL) affects less than 1 in 10,000 and is typically studied as a uniform population, even though heterogeneous pathologies and treatment outcomes have been recognized for years. As we learn in “Radiating Good Health,” through years of careful study of this patient population, Wyndham Wilson, M.D., and his team in CCR’s Lymphoid Malignancies Branch formed and tested a therapeutic hypothesis for a subpopulation with primary mediastinal B-cell lymphoma that has thus far effectively cured greater than 90 percent of patients.

Meanwhile, research efforts led by CCR’s Genetics Branch, have led to new insights into a rare subtype of gastrointestinal stromal tumors (GIST). In adults, these tumors harbor activating c-kit or PDGFR mutations and respond to kinase inhibitors targeting these receptors, but pediatric patient populations have proved more resistant to these therapies. Several years ago, CCR set up a pediatric GIST clinic to study and treat this rare subpopulation. In “The GIST of One Cancer: Two Distinct Molecular Diseases,” we learn that Keith Killian, M.D., Ph.D., Paul Meltzer, M.D., Ph.D., and their colleagues have identified distinct epigenetic changes in the tumors



(Photo: R. Baer)

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of these patients associated with succinate dehydrogenase mutations.

Bladder cancer might not be rare, but it has not drawn commensurate interest from researchers; no new therapies have been approved for bladder cancer in 25 years. CCR has recently set up a program to advance the treatment of bladder cancers, which is beginning to yield promising results. Andrea Apolo, M.D., and Piyush Agarwal, M.D., give a first account of this program in “Treating Bladder Cancer: From Primary Tumor to Metastasis.” The story of patient Chris Hamilton that accompanies this article reflects the challenges and a sense of the possibilities for patients with this and other under-investigated cancers.

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