In just a few years, immunotherapy has become one of the biggest stories in cancer care. Some of the earliest clinical trials, as well as work on the biomarkers critical to these revolutionary treatments, were done at Yale.

“Immunotherapy can be used in many different tumor types, so the potential to treat a large number of patients across a range of cancer types is massive,” says Kurt Schalper, MD, PhD, Assistant Professor of Pathology and Director of the Translational Immunology Laboratory. “We realized there would be a great need for translational science to understand the biological determinants and explore the potential of novel immunostimulatory therapies, including identifying predictive biomarkers that could improve patient care.”

With research into biomarkers and immunotherapy surging at Yale Cancer Center, Dr. Schalper and others started developing standardized protocols and quantitative methods to carefully evaluate anti-tumor immune response. Simultaneously, they discussed strategies to meet the demand for high-quality tumor samples for research and support of translational studies for immuno-oncology clinical trials. The result was Dr. Schalper’s Translational Immunology Laboratory.

Previously, if a Yale researcher wanted to undertake a project requiring interrogation of immune markers in tumor samples, that scientist had to contact different investigators from diverse laboratories, departments, and “core” service facilities. Coordination was limited, frequently leading to inefficient use of samples and limited comparability across studies.

“It was difficult to know where to start and how to optimally integrate and communicate all the data,” explains Dr. Schalper, “and also difficult to pull together a single project budget. We decided to standardize relevant immun-oncology studies, harmonize protocols, and funnel the work through a single place.”

For example, Dr. Schalper is currently interacting with and supporting immune related molecular studies in diverse tumor types including lung, bladder, breast, head and neck, and digestive tract malignancies. He is also involved in projects with industry partners, in multi-institutional academic projects, such as AAcR’s Stand Up To Cancer Lung Cancer Dream Team, and meets regularly with members of the Yale SOPERE in Lung Cancer to discuss projects and to review and manage the tissue samples needed. All of which may require immunophenotyping, measurement of functional immune markers, analyses of nucleic acids, and integrated biostatistics and bioinformatics.

“We marry the researcher’s idea or the clinical project needs with an opportunistic biospecimen collection plan and execute or guide state-of-the-art anti-cancer immunology molecular studies,” says Dr. Schalper. “Not infrequently, it’s a reality check between what the researchers aim to do and the resources that are required to get the job done.”

Asking the right questions beforehand is crucial. Does the study require blood or tumor tissue collection? Is tissue fresh, frozen, or fixed? If fresh, do they know how to preserve it after taking it from the patient? What sort of assays best suit the project’s purposes? Optimal execution of translational projects require careful planning, technical knowledge of the advantages and limitations of laboratory methods, and capacity to accurately estimate the associated costs and potential problems.

“If samples aren’t prepared correctly or stored correctly, the researcher may miss an opportunity,” says Dr. Schalper. “Or if they’re measuring T-cells, some markers only measure the presence of the cells, some markers assess the function of the cells, and sometimes you have to do a combination.”
"We marry the researcher’s idea or the clinical project needs with an opportune biospecimen collection plan and execute or guide state-of-the-art cancer immunology molecular studies."

“If an investigator isn’t familiar enough with the technical aspects of the proposed assessments, you may get, for example, DNA sequencing data that doesn’t match up, or the wrong type of sequencing to compare. This has to be coordinated up front, and there has to be enough knowledge about each of the different assays to make sure that at the end of the project, the data from each of those assessments can support each other and you can make conclusions about it,” adds Edward Kaftan, PhD, Associate Research Scientist, who helped Dr. Schalper launch the Translational Immuno-oncology Lab.

Careful planning is also essential to ensure that tumor samples are used efficiently. Researchers who aren’t quite clear about their goals or methods can waste tissue and/or exhaust limited sample supplies before all the necessary assays are done.

“Tissue samples are highly precious,” says Dr. Schalper. “They’ve become smaller and smaller over the years because of advances in medical technology and imaging, so we typically don’t receive big biopsies. The samples are shrinking but the number of questions and studies we have are growing. That’s why we need to coordinate the science with the collection of the sample in the right way.”

Dr. Schalper also helps researchers estimate a budget. It’s another reality check best done beforehand. Researchers often don’t understand the costs of the various assays, or whether they can be done at Yale or must be outsourced. Dr. Schalper has much of this information, collects the rest, and advises the investigator as to what the project will cost and how long it will take.

“Having an early and clear view about the costs associated with the project is crucial to support the execution and success. This also helps adjusting to particular funding sources or requirements.”

After the planning comes the execution when all the assays and lab work are performed. Dr. Schalper coordinates this as well, and in many cases the assays are completed in his lab. When the projects need high throughput genomic sequencing, they are executed in the Yale Center for Genome Analysis or with external partners, but quality-control and analysis is completed by a Yale bioinformatician to make sure the analyses are standardized across samples, and to ensure the accuracy and comparability of the data.

Meanwhile he and his research team are looking ahead. They have validated assays for over 30 immune related biomarkers, and the number grows each week. “We are validating assays for the next generation of tumor targets,” he says, “which may become clinically relevant at any moment.”