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Researchers develop novel approach to visualize, measure protein complexes in tumors

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Cancer diagnosis and treatment decisions are often hampered by a lack of knowledge of the biological processes occurring within the tumor. Moffitt Cancer Center researchers have developed a new approach to analyze these processes with a technique called proximity ligation assays (PLA). PLA allows specific protein complexes to be visualized and measured in cancer specimens. This may aid in patient treatment decisions in the future.

Clinical researchers and physicians often rely on measurements of cancer biomarkers as diagnostic, prognostic or treatment indicators. Cancer biomarkers are biological characteristics of tumors, such as genetic mutations, protein expression levels or protein modification events. Current biomarker analysis primarily focuses on single genes or proteins. However, proteins do not function on their own; rather, they are often part of larger multi-protein complexes and can interact with many different proteins. By only using single proteins as biomarkers, clinicians may not have an accurate description of what is actually occurring within a tumor.

Moffitt researchers developed the PLA approach in cancer specimens to analyze protein complexes and allow a better understanding of the events that occur in cancer. They focused their study on the epidermal growth factor receptor (EGFR) that is often mutated or expressed at high levels in many tumor types, including non-small cell lung cancer, head and

neck squamous cell carcinoma, and renal cell carcinoma. They discovered that lung cancer patients who were treated with EGFR inhibitors and had high amounts of EGFR protein complexes had a better prognosis.

These protein complexes may become new biomarkers to help physicians diagnose and treat patients with a certain class of drugs called receptor tyrosine kinase inhibitors. Protein complex analysis by PLA may also help physicians determine how patients become resistant to these drugs.

This work was the first step in the assessing therapy relevant protein complexes in cancer specimens. "We show that it is feasible to build assays that reflect protein complexes in cancer cells and these assays are associated with drug sensitivity. Our lab is developing additional assays reflecting protein complexes relevant to cancer therapeutics and we envision the ability to use these assays to help make therapeutic decisions for our patients," said Eric B. Haura, M.D., director of the Lung Cancer Center of Excellence at Moffitt.

"We think this is an exciting new way to look at targetable signaling activity in cancer cells. If we can figure out which molecular pathways are activated, we will be better able to match patients to available targeted therapies and hopefully improve outcomes," said Matthew A Smith, Ph.D., MSPH, post-doctoral fellow at Moffitt.

This study was published in the Jan. 13 issue of *Science Signaling* and will be discussed in a podcast on the *Science Signaling* website.

Provided by H. Lee Moffitt Cancer Center & Research Institute