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In This Issue

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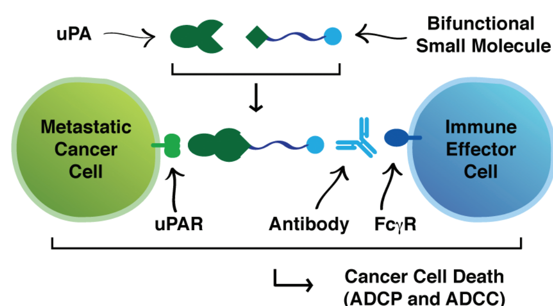
ARMING THE IMMUNE SYSTEM TO FIGHT CANCER

Over 500,000 people in the United States died from cancer in 2010, and especially deadly are cancers that have metastasized, or spread to other parts of the body. While the immune system may not be capable of killing metastatic cancer cells on its own, one promising approach to fighting cancer is to devise a method to help the immune system get rid of unwanted toxic elements. Jakobsche *et al.* (DOI: 10.1021/cb200374e) now describe a chemical strategy for luring cytotoxic agents of the immune system directly to metastatic cancer cells.

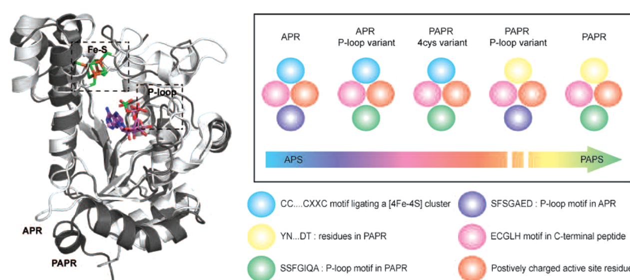


The strategy relies on the fact that many metastatic cancer cells contain higher levels of a protein called urokinase-type plasminogen activator receptor, or uPAR, on their surface than do healthy cells. uPAR binds to an enzyme called urokinase-type plasminogen activator (uPA). The authors created a bifunctional small molecule, called ARM-U, that binds to and inhibits the activity of uPA, and contains an antibody-recruiting antigen. When an ARM-U-uPA complex binds uPAR-containing cancer cells, the antigen acts as bait, luring disease-fighting antibodies to the cancer cells.

OUT OF THE LOOP

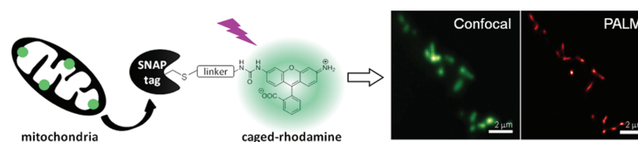
Sulfur is an important component of numerous essential biomolecules, such as the amino acids methionine and cysteine. In order to make such sulfur-containing compounds, many microorganisms come equipped with enzymes called sulfonucleotide reductases, which reduce an activated form of sulfate called adenosine-5′-phosphosulfate (APS) to sulfite. While performing this conversion, some organisms use adenosine-5′-phosphosulfate reductase (APR), and others use 3′-phosphoadenosine-5′phosphosulfate reductase (PAPR). Because there are no human enzymes that are similar to APR and PAPR, these sulfonucleotide reductases are intriguing targets for the development of new antibiotics. To better understand the factors involved in the specificities and activities of these structurally similar enzymes, Bhave *et al.* (DOI: 10.1021/cb200261n) investigate the two regions of the enzymes that differ, the P-loop and the iron-sulfur cluster.

The authors use various protein engineering, spectroscopic, and kinetic analysis methods to explore the involvement of the P-loop and the iron-sulfur cluster in enzyme function. Their data unexpectedly reveal that the iron-sulfur cluster, not the P-loop, is the major contributor to sulfonucleotide reductase specificity and activity.



SUPERRESOLUTION IN THE PALM OF YOUR HAND

Fluorescent molecules can be transformed into a non-fluorescent state when modified with an appropriate photo-cleavable compound, a phenomenon called caging. Upon activation with light, the caging group is cleaved and the fluorophore regains its fluorescent properties. Caging enables the exploration of biological processes with high spatial and temporal resolution, though subtle challenges in the technology have left a need for novel caged fluorophores that can be specifically attached to proteins of interest. Now, Banala *et al.* (DOI: 10.1021/cb2002889) report the creation of a caged rhodamine derivative that can be used for the specific labeling of SNAP-tag fusion proteins.



The caged rhodamine exploits the fact that rhodamine modified with a urea group is still significantly fluorescent. This enabled the creation of a rhodamine derivative modified on one end with a photocleavable group and on the other with a urea group linked to an O^6-benzylguanine group, which specifically reacts with proteins containing a SNAP-tag. The probe was particularly well-suited for use in photoactivated localization microscopy (PALM), in which cellular components can be imaged with nanometer resolution.

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