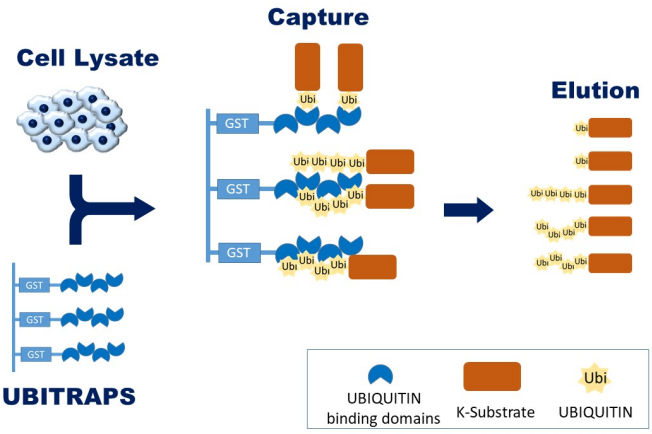
Ubiquitin-binding polypeptides

Background
Ubiquitin is a small protein with regulatory function found in most tissues. It can be covalently attached to substrate proteins (known as ubiquitination) and affects their function in different ways: 1) alter cellular location, 2) affect activity, 3) prevent interaction with other proteins or molecules and 4) mark them for degradation. Enzymes that mediate ubiquitination are involved in a multitude of human diseases such as cancer, rheumatoid arthritis, and neurodegeneration. The wide-ranging study of ubiquitination in cellular and molecular biology makes “ubiquitin binding polypeptides” or “UBITRAPS” a "must-have tool" for the daily activity of many research laboratories.
Current Options. Most of the current options for the isolation of ubiquitylated proteins involve the overexpression of a tagged-ubiquitin moiety. This overexpression might influence the ubiquitination dynamics in the cells. By contrast, the ubiquitin binding polypeptides constitute a non-invasive method. The use of ubiquitin-specific antibodies is also a non-invasive technique, but the associated expenses and expertise required for their use are prohibitive for many laboratories.

Technology
The technology is based on the linkage of multiple ubiquitin interacting motifs connected via flexible linkers, resulting in molecular “traps” with high affinity for polyubiquitin. The UBITRAPS can be used in vitro as a solid support for purification of ubiquitinated proteins, but also a tool to capture modified proteins from living cells and tissues. These ubiquitin binding peptides may also protect poly-ubiquitinated proteins from the action of deubiquitinating enzymes, therefore increasing yield.



Application
- Detection, characterization and isolation of polyubiquitinated proteins from cells and tissues for analysis, especially for proteomic studies.
- Enrichment of linear-polyubiquitinated proteins (not possible with most tagged-ubiquitins)
- Development and implementation of novel screens for biomarkers and potential for diagnostic.

Advantages
- Low nanomolar dissociation constant for chains of polyubiquitin.
- 1000 to 10,000-fold higher specificity for polyubiquitin chains over ubiquitin monomers.
- Overexpression of epitope-tagged ubiquitin for pulldowns is not necessary.
- Flexible applications and compatible with commonly used isolation technologies.

Patent Status.
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