probe. The process of fishing with the probe comprises *in situ* specific bonding of the probe compound to a protein of a living cell; *in situ* covalent crosslinking between the photosensitive group of the probe compound and its target protein under UV irradiation; specific linking of the alkynyl group of the probe compound to the azido group of the isolation compound via a click reaction; and isolating the target protein specifically bonded to the probe compound with the aid of the binding of the biotin group of the isolation compound with streptavidin-agarose bead.

Fig. 5. A tool compound for fishing of a target protein with a probe. Among the compounds tested, #50 compound exhibits the strongest ability to cause cell vacuolization. Based on an analysis of a structure-activity relationship, linking of a photosensitive group to #50 compound on a position shown in the figure to obtain a probe **#79** compound may not affect the bioactivity of #50 compound. It's also verified by experimentation that **#79** compound and #50 compound can result in the same cell phenotype. To facilitate solid phase separation and reduce non-specificity, a designed **#80** compound has a long chain linking a biotin to an azido group for a click reaction.

Fig. 6. Separation and identification of a target protein. **#79** compound used as a probe is bonded *in situ* to a target protein within a cell wherein a photo-promoted covalent linking is formed, and then reacts with **#80** compound to achieve solid phase separation and purification of the target protein. A. Left: Proteins capable of specific bonding with **#79** compound as detected by Western immunoblotting (as indicated by the arrows); right: specific target proteins separated by PAGE gel electrophoresis as indicated by coomassie blue staining. B. As shown by MALDI-mass spectrum peptide segment mapping and sequence analysis (MALDI-MS/MS), the target proteins match the known protein sequences in the data bank. The underlined bold portions are the matched sequences. The two isolated proteins of about 60 KD and about 200 KD match the same known protein sequence. C. The information of protein matching shows that the target protein of the compound is vimentin. SEQ ID NO:1

Fig. 7. Results of docking between #50 compound and the target protein. A: 3KLT (system number of the protein; the spherical portion in the center is the active region of the protein) of vimentin tetramer originated from the PDB (protein data bank); B: #50 compound for docking; C: scores of the top 10 configurations of #50 compound resulting from docking between 3KLT and #50 compound using software Discovery Studio 3.0 and the LibDock docking method therein; D: a view showing the interaction between the #50 compound configuration having the highest score (indicated by purple color) and vimentin; E: amino acids forming hydrogen bonds with #50 compound after deproteinization, wherein the two