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New findings on heat shock proteins may shed light on variety of debilitating diseases

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UCLA researchers, in a finding that runs counter to conventional wisdom, have discovered for the first time that a gene thought to express a protein in all cells that come under stress is instead expressed only in specific cell types.

The group, from the Jules Stein Eye Institute and UCLA Pulmonary and Critical Care Medicine, focused on αB-Crystallin, a small heat shock protein. Heat shock proteins are a class of functionally-related proteins involved in the folding and unfolding of other proteins. Their expression is increased when cells are exposed to taxing environmental conditions, such as infection, inflammation, exercise, exposure to toxins and other stressors.

αB-Crystallin may be associated with certain cancers and could be developed into a biomarker to monitor for diseases such as multiple sclerosis, age-related macular degeneration, heart muscle degeneration and clouding of the eye lens. Any discoveries about how this protein is regulated and its molecular biology may reveal potential targets for novel therapies, said study first author Zhe Jing, a research associate in UCLA Pulmonary and Critical Care Medicine.

"If you use a certain cell type, this protein can be induced when the cells are stressed, but that doesn't happen in a different cell type," said Jing. "This novel finding does conflict with what has been thought, that this protein could be induced in any cell type."

The findings of this two-year study are published in the most recent issue of the journal *Cell Stress and Chaperones*, a peer-reviewed journal in the fields of cell stress response.

The UCLA team did the study using four cell lines – two epithelial cells lines and two fibroblast cells lines. They found that the protein cannot be induced by stress in epithelial cells, in which 80 percent of cancers arise. It can, however, be induced in the fibroblasts that make up muscle tissue.

The significant finding in this investigation is that, in certain cell types, only one specific heat shock factor controls the expression of αB-Crystallin. For example, in the epithelial cell lines, it is heat shock factor 4 (HSF4), while a different heat shock factor, (HSF1), plays this role in the fibroblast cells lines.

In the past, the data has indicated that a heat shock factor could control the expression of αB-Crystallin randomly and equally. However, Jing's discovery overrides this rule. His findings strongly suggest the "preference" of the αB-Crystallin to heat shock factors in certain cells may be correlated with its versatility to various diseases.

"Considering the multiple roles of αB-Crystallin in so many diseases, the access of the HSF1 and HSF4 to the αB-Crystallin gene dictated by the certain cell type may be what is helping to cause certain diseases," Jing said. "If we can uncover the cascade of events that result in disease, we may be able to come up with strategies to block or interrupt that cascade."

Going forward, Jing and the research team will validate what they found in this study by examining single cells, which provides a greater challenge but may lead to further discoveries.