The UBE2G2 Binding Domain in the Ubiquitin Ligase GP78 and Methods of Use Thereof

Summary (1024-character limit)
Researchers at the National Cancer Institute (NCI) have developed an invention describing the binding domain (G2BD) for the ubiquitin-conjugating enzyme Ube2G2 in the gp78 ubiquitin ligase protein. The invention involves modulating the interaction between the gp78 protein and the conjugating enzyme Ube2G2. Interruption of this interaction will block degradation from the endoplasmic reticulum (ER), resulting in ER stress, unfolded protein response, and, ultimately, apoptosis in some cancer cells. The NCI seeks licensing and/or co-development partners for this invention.

NIH Reference Number
E-244-2004

Product Type
- Therapeutics

Keywords
- Cancer, Metastasis, Apoptosis, Ubiquitin, Ube2G2, gp78, Endoplasmic Reticulum, ER, Stress, ER-associated Degradation, ERAD, Weissman

Collaboration Opportunity
This invention is available for licensing and co-development.

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Description of Technology
Cancer is the second leading cause of death worldwide. The primary cause of mortality from cancer is metastasis. While the underlying mechanisms of cancer metastasis are still being unraveled, the gp78 protein involved in ER-associated degradation (ERAD) appears to play a role in metastasis in sarcoma. Targeting gp78 may be a therapeutic option in cancer treatment.

The prometastatic activity of ERAD requires the E3 ubiquitin ligase activity of gp78. Gp78 targets the transmembrane metastasis suppressor, KAI1, for degradation. Suppression of gp78 results in the accumulation of KAI1 and a reduced metastatic potency of sarcoma cells.
Regulating gp78 presents a new therapeutic strategy for the treatment of sarcomas. The National Cancer Institute (NCI) is seeking statements of capability or interest from parties interested in licensing or in collaborative research to co-develop technologies that disrupt gp78 activity and/or ERAD activity for the treatment of cancer.

**Potential Commercial Applications**
- Targeted therapies for sarcomas, melanoma, breast cancer, myeloma and other solid tumors and leukemias
- Reducing activation of SREBP pathway for lipid and cholesterol synthesis
- Reducing degradation and improving maturation of cell surface or secreted proteins
- Developing a method to identify more robust gp78 inhibitors

**Competitive Advantages**
- The G2BR is the only reagent specific for targeting the endoplasmic reticulum-associated degradation E2, Ube2G2

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**Development Stage**
- Pre-clinical (in vivo)

**Publications**
- Chen B et al. The activity of a human endoplasmic reticulum-associated degradation E3, gp78, requires its Cue domain, RING finger, and an E2-binding site [PMID 16407162]
- Tsai YC et al. The ubiquitin ligase gp78 promotes sarcoma metastasis by targeting KAI1 for degradation [PMID 18037895]
- Das R et al. Allosteric Activation of Ubiquitin Ligase Activity by a Structurally-Defined Specific E2 Binding Region of gp78 [PMID 19560420]

**Patent Status**
- **U.S. Provisional:** U.S. Provisional Patent Application Number 60/583,263 , Filed 26 Apr 2004
- **U.S. Patent Filed:** U.S. Patent Application Number 8,420,776 , Filed 16 Apr 2013

**Therapeutic Area**
- Cancer/Neoplasm