S-allylcysteine for Use in the Prevention and Treatment of Plasma Cell Dyscrasias

A treatment strategy for prevention of progression of SMM/MGUS to MM without the serious side effects of painful peripheral neuropathy.

Technology

Myeloma plasma cells is characteristic of large quantities of paraprotein that they synthesize and secrete, rendering them sensitive to ER stress. The inventors designed a specific screen to pick out compounds that disrupt protein secretion. The screen employs Gaussia luciferase (Gluc) that can be easily monitored through extra cellular release of luciferase activity in real time and detects decreased protein processing in the secretory pathway as a measurable hallmark of ER stress. Two MM cell lines expressing Gluc were exposed to compounds in natural library to enable identification of those that potentially induced ER stress as measured by inhibition of Gluc. SAC was identified as the top hit, which like BTZ, disrupts protein equilibrium in the ER by preventing degradation of misfolded proteins. Multiple assays by the inventors have proven that SAC promotes ER stress and arrests proliferation in MM cells, thereby making it a lucrative candidate for MM and myeloproliferative disorders sans the side effects.

Background

Monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) are asymptomatic myeloproliferative disorders, a condition where the bone marrow produces too many blood cells. Approximately 5% of the population above the age of 50 are affected and have a 15 to 59% lifetime risk of eventually progressing into an incurable malignancy called multiple myeloma (MM). Currently, there are no drugs to prevent this progression and the patients are just continually monitored for plasma markers. Patients progressing to MM are treated with a proteosome inhibitor, bortezomib (BTZ) to which remarkable response rates have been demonstrated. Due to the similarity in innate biology of MM providing sensitivity to BTZ via the ER stress pathway and also biological similarities between MM and SMM, BTZ is predicted to have good out come in the management of MGUS and SMM. But BTZ causes painful peripheral neuropathy in more than 30% of the patients and is not a preventative solution. Even though Takeda pharmaceuticals have now received FDA approval for subcutaneous administration of BTZ to reduce nerve damage, there is a pressing need for an oral alternative as it is preferred for long term administration. Therefore, the inventors have identified an alternative compound S-allyl cysteine (SAC) which is naturally found in garlic through a unique screen for agents disrupting protein secretion and like BTZ, targets the ER (endoplasmic reticulum) stress pathway. This agent has the potential not only to treat MM, but also to prevent the progression of SMM/MGUS to MM.

Applications

Technology ID

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Category

Life Sciences/Therapeutics/Oncology

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Learn more

- The treatment of multiple myeloma (MM)
- Myeloproliferative disorders / Plasma cell dyscrasia: Prevention of the progression of Monoclonal gammopathy of undetermined significance (MGUS)/smoldering multiple myeloma (SMM) to MM

Advantages

- A natural compound alternative to the current first line of treatment for MM
- There are currently no treatment strategies for prevention of MGUS/SMM progression to MM and the patients are only monitored via plasma markers. SAC is the first natural compound alternative identified that can be orally administered for prevention
- Targets the same pathway as the current treatment strategy available but without the debilitating side effects of painful peripheral neuropathy
- Administration can be carried out orally, which is a sustainable long-term option as the treatment strategy involves long term follow up

Intellectual Property

A U.S. non-provisional patent was issued related to the use of S-allylcysteine in order to treat plasma cell dyscrasias.