ABSTRACT

MODIFIED MEMBRANE TYPE SERINE PROTEASE 1 (MTSP-1) POLYPEPTIDES AND METHODS OF USE

Provided are MTSP-1 polypeptides modified to have altered activity and/or specificity so that they cleave a complement protein, such as complement protein C3, to inhibit its activity and thereby inhibit complement activation. The modified MTSP-1 polypeptides that inhibit complement activation can be used for treatment of diseases and conditions in which complement activation plays a role. Such diseases and conditions include inflammatory diseases and diseases with an inflammatory component. Exemplary of these disorders are ischemic and reperfusion disorders, including myocardial infarction and stroke, sepsis, autoimmune diseases, ophthalmic disorders, such as diabetic retinopathies and macular degeneration, including age-related macular degeneration (AMD), and transplanted organ rejection, such as renal delayed graft function (DGF).

(Figure 1)