COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

7-day Prophylactic Antiviral Patch With Host-based MOA and Broad Spectrum Protection

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Our goal is to provide a broad-spectrum prophylactic antiviral patch to the Joint Force across the globe. This transdermal drug in adhesive patch will provide protection from a wide range of viral infections for 7-days at which point the Warfighter can easily apply a new patch to continue viral protection. The drug in adhesive type patch is durable and economically scaled by our leading CDMO.
CFD Research's antiviral program is currently funded through a CBD Phase II SBIR and the DTRA/Battelle Batcave program. CFD Research has established a medicinal chemistry program around a novel thiazole-2-carboxamide (TC) scaffold (MW 250-370). The TC series possesses optimal transdermal properties such as MW ~ 300, tPSA ~ 30, LogP ~ 3.0 and high synthetic tractability. Fifty analogs have been made to date which have improved potency against VEEV and CEV by more than 10-fold. The TC series has been tested for in vitro potency by USAMRIID, utilizing their mcroscopy based assay. Additionally, cytopathic effects and luminescence-based assays have confirmed antiviral activity. Thus far, broad prophylactic activity (0.8 - 6 uM) has been demonstrated in alphaviruses (VEEV), bunyaviruses (CEV,HNTV, RVFV,LASV), and mononegavirales (NIPV). The broad antivirial activity is achieved through a host-based mechanism of action. Previous studies have demonstrated that similar scaffolds inhibit pyrimidine biosynthesis. Our scaffold's putative target is UMP synthetase based on metabolomic studies of pyrimidine precursor accumulation. Viral replication has been shown to depend on host pyrimidine biosynthesis. Additionally, pyrimidine synthesis inhibitors have been shown to amplify the innate immune response through induction of 2'-5'-oligoadenylate synthetase like (OASL) which enhances type 1 interferon production. Cytotoxicity studies have shown that the TC series is not toxic up to the max tested concentration of 60 uM.
Future work includes animal studies with the patch in species higher than rodents to attain the innate immune activation response. Formulation and CMC finalization with our CDMO. GLP toxicology studies and MOA studies to support an IND submission.

CBD SBIR and DTRA