Grand Challenges Explorations Application Form

Please enter proposal text in Sections I and II, according to the instructions within each section. Click on the shaded text and begin typing – you may type over the instruction text to save space. If you choose to include charts and graphs, add them within the appropriate section.

Your application must fit into 2 pages in 11 point font and be less than 2000 words. The entire file should be less than 2MB. Proposals that exceed these restrictions may be blocked from submission and will not be reviewed.

Section I. The Idea

In this section please explain the idea or approach that addresses the topic. Discuss why the idea is innovative or unique and the objectives that will be accomplished.

Crowdsourcing is a term introduced by Jeff Howe to describe the solution of problems through a distributed network of people. Although there are several examples of crowdsourcing in science, most are not open. The best known example is Innocentive, where scientific problems are made public with prizes for the solvers. However, the proposed solutions are not made public and accepted solutions are intended to be proprietary to the company funding the solution. Innocentive is also collaborating with the Rockefeller Institute for help to combat third world and orphan diseases. Other non-commercial examples in science include Stadust@home and GalaxyZoo, initiatives designed to identify astronomical objects. Some recent examples of crowdsourcing in chemistry are Chemmunity, the Synaptic Leap, OrgList, Chemists Without Borders and ChemUnPub.

The term "Open Notebook Science" was coined to represent a form of Open Science where the laboratory notebook is made public in as close to real time as possible. The Bradley lab has demonstrated the feasibility of carrying out Open Notebook Science since the summer of 2005 with the UsefulChem project (http://usefulchem.wikispaces.com). Experiments are stored on wiki pages, much like in a paper notebook, but with hyperlinks to all the raw data collected. There is also a blog (http://usefulchem.blogspot.com) to report on the overall progress of the scientific work. The blog and wiki receive about 200 hits per day. Over time, a collaboration with other scientists has evolved. Rajarshi Guha at Indiana University and Tsu-Soo Tan from Nanyang Polytechnic in Singapore have invested significant amounts of time in running docking calculations for UsefulChem virtual libraries and reporting their results openly, in near real-time. Dan Zaharevitz, from the National Cancer Institute has contributed by testing compounds for potential anti-tumor activity. Phil Rosenthal, from UCSF, has tested compounds for anti-malarial activity. Other individuals from around the world have contributed by engaging in open discussions in the blogosphere. The UsefulChem project has also been cited in the peer-reviewed literature.

The core idea of this proposal is that fighting resistance to current anti-malarial drugs depends upon the ability of the scientific community to quickly develop compounds and document their properties. By reporting on research using Open Notebook Science in addition to conventional publication vehicles, this process can be accelerated. Not only can actively collaborating groups gain more insight into the experimental difficulties but people not initially targeted as potential contributors can discover the live research and participate. This is where the power of crowdsourcing can really come to bear, as it has in many other fields.

Section II. Project Design and Implementation Plan

Please briefly describe the project design and implementation plan you will follow to complete this phase of the project successfully. If there are new technologies or tools to be developed or introduced in the project, please provide a concise technical description.

You do not need to complete the proof-of-concept for your idea in Phase I. However you must show credible evidence supporting the validity of your idea and give sufficient proof to warrant expanded support. In addition you should describe what the next steps for this project.

During the exploratory first year, funds will be used to achieve the following objectives:

1) Support students and materials to carry out the synthesis of new compounds, extending the strategy of generating Ugi products, which has worked well thus far in identifying 2 compounds with moderate anti-malarial properties. The focus is on making compounds that are available from low cost starting materials and can be purified by crystallization, thus ensuring that any useful compounds can be made cheaply and quickly on any scale.
2) Support for in vitro testing of anti-malarial activity of synthesized compounds.
3) Support to perform docking and QSAR calculations to prioritize the order of synthesis of compounds from virtual libraries of Ugi products. These will include docking against enzymes, such as falcipain-2, that are likely to be valid targets for strains of Plasmodium falciparum resistant to common anti-malarial drugs.
4) Support for collaborators in the form of prizes for meeting targeted objectives. For example, an award will be shared by the first individuals to participate in the calculation, synthesis and testing of a new compound with anti-malarial activity equal or surpassing that of existing documented inhibitors for a given enzyme target.
5) The PI will actively coordinate the activities of the collaboration and ensure that detailed experimental data are made freely available in as close to real time as possible on the UsefulChem wiki. Reports of progress, challenges, opportunities and milestones related to this project will be reported on the UsefulChem blog as well as relevant social software networks where biomedical researchers communicate.

During the next stage of funding, the scope of the project will be expanded to incorporate an automated reaction system (such as available from ChemSpeed or Mettler-Toledo). Experiments currently performed manually or semi-manually will be adapted to the new system to enable a significant increase in throughput.

Projects and experiments suggested by the crowdsourcing community to assist in attacking resistance to anti-malarial compounds will be evaluated and resources will be allocated to execute the experiments, under supervision of the PI. As sub-projects get completed, work will be submitted for traditional peer reviewed publication. Arguments in the papers will be supported by links to the original experiments in the online open notebook wiki, giving unprecedented systematic access to experimental raw data to be re-analyzed or re-purposed by anyone. Co-authorships will be based on documented contributions from members in the community who sufficiently participated.

From the larger perspective a key outcome of this project is the establishment of a precedent and model to demonstrate how crowdsourcing can be used to solve scientific problems openly. A case can be made that transparency can lead to higher efficiency in scientific progress. However, a working model is just as important as the willingness of the researchers to participate.