**eMERGE Network Proposal for Analysis**

Project/Manuscript Concept Sheet

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| **Submission Date** | July 18, 2016 |
| **Project Title** | MEdicine Gene Annotation (MEGA): A REDCap based tool to support consensus variant interpretation  |
| **Tentative Lead Investigator (first author)** | Wayne H. Liang1 |
| **Tentative Senior Author (last author)** | David R. Crosslin1 |
| All other authors  | Gail P. Jarvik1Bas de Veer1Any eMERGE investigator interested in the project. |
| **Sites Involved** | 1Group Health/University of Washington |
| **Background / Significance** | The interpretation of clinical utility of genetic variation has proven to be a difficult task with diverse results. Presently, there are only a fraction of genes (∼200) of the estimated ∼19,000 that are deemed actionable, and that is only on single nucleotide variation (SNV), small insertions/deletions (indels) or copy number variation (CNVs). We are proposing a system to help survey and manage genetic variant interpretation. MEdicine Gene Annotation (MEGA) is a portable, openly available tool which supports the process of arriving at a consensus variant interpretation within a group of multiple individuals. The workflow includes parsing scripts to extract variant information from a single or multisample VCF. These data will be stored and managed using R Project for Statistical Computing and SQLite (RSQLite) in a relational data base format to assist with a dynamic updating system. We will push the variant and survey data to REDCap using their API, providing a seamless flow of data exchange. From REDCap, an automated email will be sent to multiple individuals inviting the users to click on a link. The link will take the user to the MEGA interface, where they can input their opinion on specific variants in a simple interface as well as see other user’s opinions. They will be able to complete the survey with no log-in required. Reminder emails can be scheduled directly from REDCap. Once completed, data are collected directly in REDCap and can be programmatically accessed via the same API interface for pushing data. Individual opinions on each variant will be visualized in tabular and graphical formats to provide feedback to the group in order to achieve consensus. Finally, a final consensus interpretation can be entered which will be saved within REDCap. We will use an iterative, participatory design process involving users who are involved in the process of variant annotation. The tool will be written in PHP, HTML, and CSS and will be published as a REDCap plugin.  |
| **Outline of Project** | 1. Background on challenges with variant interpretation
2. Application testing and evaluation
3. Publish manuscript
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| **Desired****Variables (essential for analysis****indicated by \*)** | * Description of design process
* Description of user feedback
* Description of user evaluation
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| **Desired data** | User feedback on prototype iterations.User evaluation of the application |
| **Planned Statistical Analyses** | None |
| **Ethical considerations** | None |
| **Target Journal** | An applied bioinformatics journal, to be determined. |
| **Milestones\*\*** | June 2016 – Presented with eMERGE Annotation workgroupJuly 2016 – Invite user participants/co-authorsJuly-Sept 2016 – Iterative prototyping and user feedbackSept-Oct 2016 – Application testing and evaluation |

**\*\*** This section should include: Timeline for completion of project, including approval, project duration, first and second draft of the paper and submission.