

Common Fund Idea Nomination Template

Title of proposed program: Using Pharmacogenomics to Improve Opioid Pain Management

What is the major obstacle/challenge/opportunity that the Common Fund should address?

Opioid analgesics are the widely used to treat pain. However, opioid analgesics have a narrow therapeutic index with many adverse effects and often do not provide adequate pain relief. The adverse effects that can be associated with opioid analgesic administration include euphoria, hyperalgesia, nausea, constipation, drowsiness, dizziness, pruritus, respiratory depression, withdrawal (somatic and affective symptoms), and addiction. Large individual differences exist in opioid analgesic efficacy and adverse effects. Genetic factors affecting pain pathways, pain perception, analgesic metabolism (pharmacokinetics), transport and receptor signaling account for some of these large individual differences. The identification of genetic factors affecting the efficacy of opioid analgesics and their adverse effects will greatly improve and personalize pain management with opioid analgesics by maximizing analgesia and decreasing side effects.

What would the goals of the program be? The goal of the program is to personalize opiate analgesic pain management using pharmacogenomics to maximize treatment efficacy while decreasing adverse events.

Why is a trans-NIH strategy needed to achieve these goals? Pain is a symptom common to all most all diseases and a significant part of the mission of the large majority of IC's at the NIH. Large sample sizes are needed for pharmacogenomics studies to identify gene variants associated with the efficacy opioids in providing relief from different the wide array of pain associated with each disorder, and are needed for replication. No single IC has the resources or access to different patient populations to study pain patients the majority of pain conditions. The initiative would also help to harmonize different measures of pain.

What initiatives might form the strategic plan for this topic?

An RFA using a U01 mechanism totaling \$10 million is proposed for this initiative. The efficacy of treatment of different types of opioid analgesics for chronic pain would be assessed. The adverse effects associated with opioid analgesic include euphoria, hyperalgesia, nausea, constipation, drowsiness, dizziness, pruritus, respiratory depression, withdrawal (somatic and affective symptoms), and drug interaction would also be assessed. The PK/PD of the prescription opioids will be measured. Blood will be collected to identify gene variants associated with the efficacy of treatment and the occurrence and severity of adverse events. As part of this initiative a PhenX measures for pain and side effects will be developed.

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A second initiative will be funding of R25 mechanisms for genomic medicine implication such as physician training. The R25 mechanism would support training courses on opioid pain management and the use the R25 will also support the integration of pharmacogenomics of opioid pain management into the curriculum of medical and nursing schools and into medical residency programs.

If a Common Fund program on this topic achieved its objectives, what would be the impact?

The use of pharmacogenomics to optimize opioid pain management would increase the efficacy of the treatment of pain and decrease the number of deaths due overdose and the number of emergency room visits by giving opioids to those who will benefit and reduce unwarranted side effects. This initiative to improve opioid pain management will significantly mitigate the economic cost of chronic pain, totaling \$600 billion dollars per year. By prescribing opioid analgesics to only those who will benefit, a significant reduction of in the number and amount of opiates prescribed is expected to result in decreased prescription opiate abuse by limiting availability. Furthermore, by decreasing adverse effects of opioid analgesics and reducing availability the half million emergency rooms visits and the 16,000 deaths in the United States will be greatly reduced, saving more than \$72 billion dollars per year.

This initiative would help accomplish the goals Patient–Reported Outcome Measurement Information System (PROMIS®), and the goals of comparative effectiveness research to measure treatment effectiveness.