MetaCensus: a blockchain meta-analysis network to improve scientific consensus and clinical decision support in pharmacogenomics

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BACKGROUND

Consensus development and effective data summarization are two barriers limiting clinical utilization of pharmacogenomics. Easy access to clear, concise, and peer-reviewed evidence for clinicians to review is central to addressing these barriers.

Meta-analyses are the gold standard for clinical consensus in medicine. Conventional meta-analyses are static publications with re-analysis published every 2 to 3 years that often have inconsistencies in inclusion decisions that are not stored in a centralized open-access repository. To address these barriers, we report our efforts to build MetaCensus, the first blockchain meta-analysis database of gene-drug pairs to support clinical consensus around and utilization of pharmacogenomics.

METHODS

Between January 2004 and January 2022, PubMed, EMBASE, and Cochrane were reviewed for meta-analyses on *UGT1A1*-irinotecan and *DPYD*- fluoropyrimidines.

Data from all studies included in meta-analyses were abstracted and uploaded to a Drupal database. A Private Ethereum Blockchain network is being built to allow interested stakeholders to apply to become a new node on the blockchain database. The existing nodes on the inclusion protocol may vote to approve a new node and the inclusion of studies submitted for review. Studies meeting threshold voting consensus for inclusion will be added to the meta-analysis, reflecting the new data and logging the changes in results, which will become available for others to review and incorporate into clinical decision support (CDS) tools.

RESULTS

A total of 1,361 articles were identified in our literature search: 15 meta-analyses containing 38 individual studies were identified for Irinotecan toxicity (grade 3 to 4: neutropenia and diarrhea) associated with *UGT1A1*, and 7 meta-analyses, comprising 37 individual studies, were identified for fluoropyrimidine toxicity (grade 3 to 4: hand-foot syndrome, hematological, and GI) associated with *DPYD* (**Figure 2**). As seen in **Figure 1**, no two meta-analyses included the same studies during overlapping time periods between two meta-analyses. Also included were ten studies published after the most recent meta-analyses for *UGT1A1*-related toxicity with irinotecan.

All studies have been uploaded to the Drupal database (QR codes 1 and 2) for initial voting on inclusion in MetaCensus after voting members develop an inclusion protocol following the Preferred Reporting Items for Reviews and Meta-analysis (PRISMA) guidelines. A MetaCensus member application webpage is being developed to recruit interested voting and non-voting members (QR code 3).

Figure 1. Comparison of studies incuded in *UGT1A1* -irinotecan meta-analyses

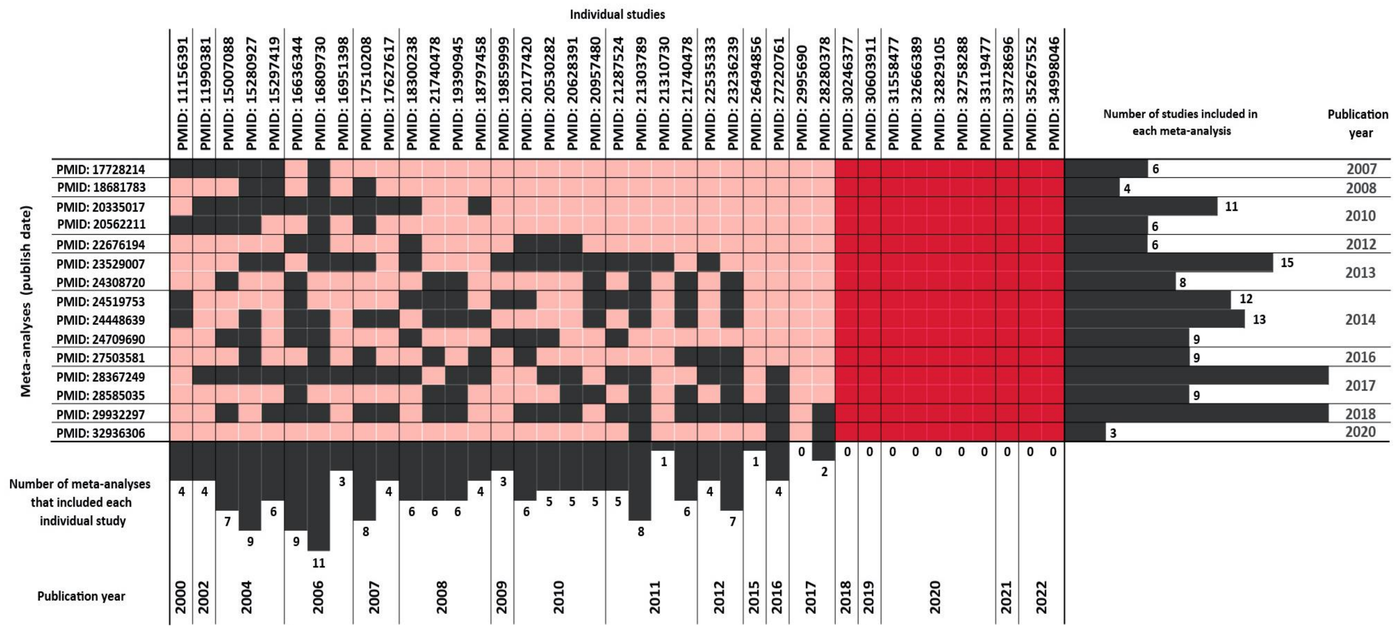


Figure 1. Comparison of studies incuded in *DPYD* -fluoropyrimidine meta-analyses

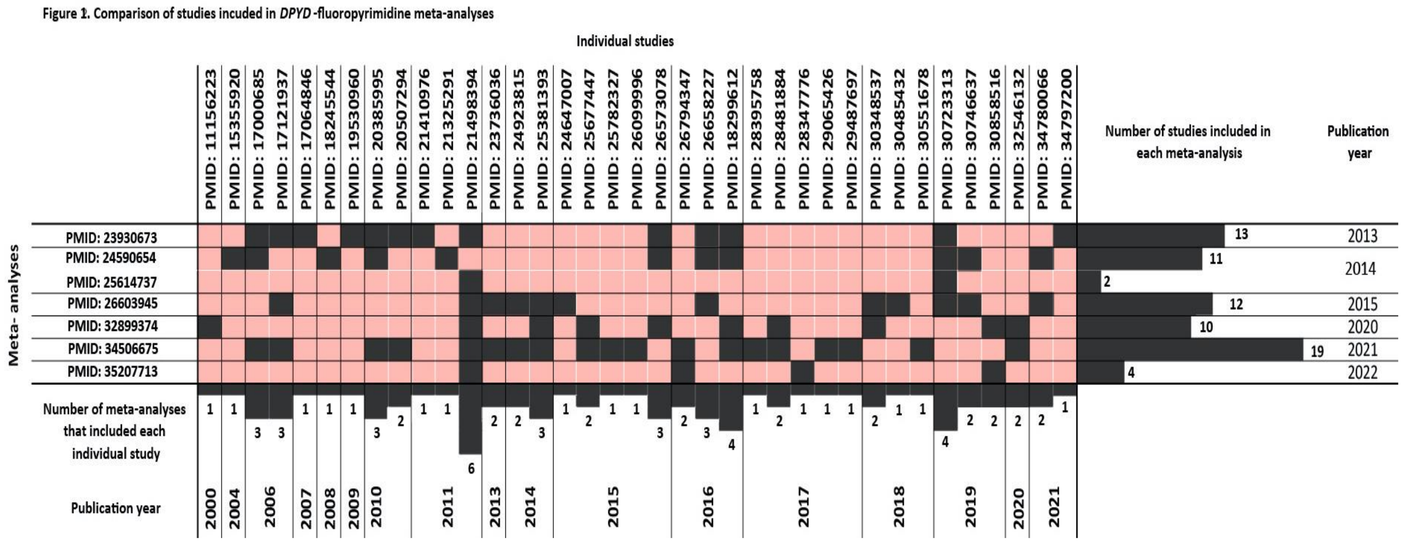


Figure. 3: Flowchart of the studies identification and selection process.

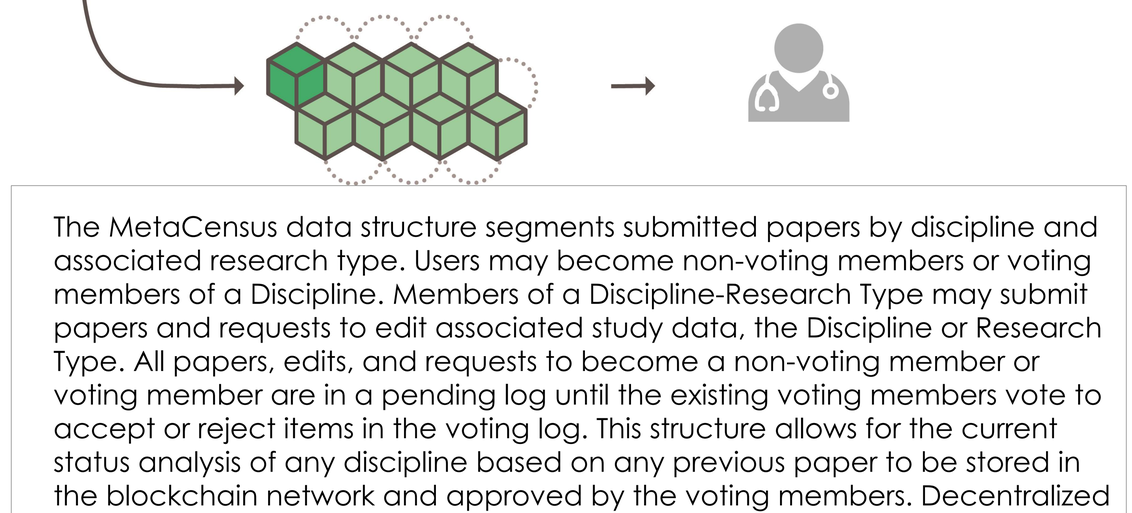
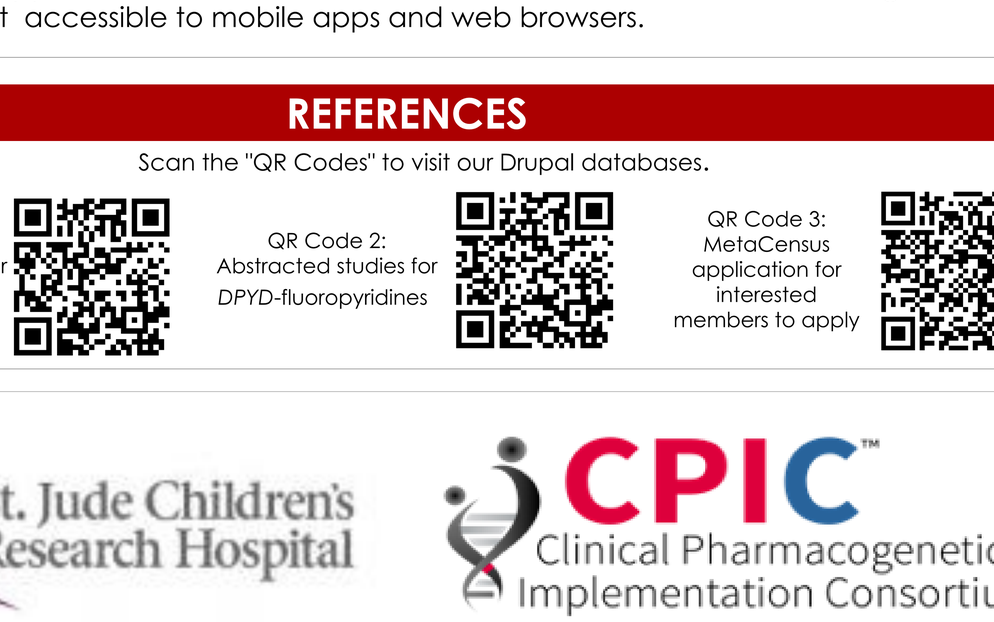


Figure. 4: A generalized workflow of the blockchain methodology.



The MetaCensus data structure segments submitted papers by discipline and associated research type. Users may become non-voting members or voting members of a Discipline. Members of a Discipline-Research Type may submit papers and requests to edit associated study data, the Discipline or Research Type. All papers, edits, and requests to become a non-voting member or voting member are in a pending log until the existing voting members vote to accept or reject items in the voting log. This structure allows for the current status analysis of any discipline based on any previous paper to be stored in the blockchain network and approved by the voting members. Decentralized apps will be able to connect to these MetaCensus data, rendering it accessible to mobile apps and web browsers.

CONCLUSION

Utilizing a blockchain-based database, MetaCensus is intended to enhance collaboration, promote PGx community involvement, accelerate consensus, and expand the use of clinical decision-making tools. As an open-access network, MetaCensus has been designed to be free to access and necessitates community involvement and contribution to accelerate scientific and clinical consensus through meta-analyses.

REFERENCES

Scan the "QR Codes" to visit our Drupal databases.

QR Code 1: Abstracted studies for *UGT1A1*-irinotecan

QR Code 2: Abstracted studies for *DPYD*-fluoropyridines

QR Code 3: MetaCensus application for interested members to apply

ARUP LABORATORIES

Pharmacogenomics GLOBAL RESEARCH NETWORK

St. Jude Children's Research Hospital

CPIC™ Clinical Pharmacogenetics Implementation Consortium