Introduction

NCBI creates the Medical Genetics Summaries (MGS) to provide information on the genetics of drug response or diseases to support the Precision Medicine Initiative. MGS is a bookshelf entry that synthesizes pharmacogenomic information from authoritative sources, such as FDA, professional practice guidelines and literature. Its content incorporates standardized nomenclatures and computational tools that makes them compatible for integration in electronic health records (EHR) and hospital systems. MGS will help clinicians who seek practical, evidence-based information to use in clinical care settings.

MSG integrates tightly with other NCBI resources that can be utilized in the realm of precision medicine, such as molecular data related to the human genome and biomedical literature resources. MGS content undergoes formal review process and is regularly updated. This service will continue to evolve along with the Genetic Testing Registry (GTR) and MedGen (two related resources at NCBI) to offer healthcare providers updated information.

Access And Term of Use

MGS is freely available from the NCBI Bookshelf (A). The table of contents display (partially collapsed) allows easy browsing of the conditions covered. The search box (B) enables searching with text terms related to specific disease, or drug, of interest. The portlet in the upper right hand corner (insert, C) provides alternative display formats and a PDF download link. Relevant sections of MGS are also available through links from selective records in GTR and MedGen (D).

No permission is required to reproduce/redistribute the collection (E), but appropriate attribution should be given using the “Cite this Page” information (F).

Using MGS Service

An MGS summary can serve clinicians in several ways. Representative usage includes:

- finding pharmacogenetics information related to an individual drug
- finding genetic components for diseases
- accessing information on tests
- interpreting test results into actionable therapy
- further in-depth investigation into precision medicine through links to other NCBI resources

GTR, a database of orderable clinical genetic tests
MedGen, a portal to information about phenotypes with a genetic component

https://www.ncbi.nlm.nih.gov/books/NBK61999
MGS Use Cases

We will describe the functions MGS provides by presenting a few usage examples.

Use Case 1: Locate information relating to pharmacogenetics of colorectal cancer treatment.

Searching MGS for “colorectal cancer” retrieves several summaries, and one of them is on “Irinotecan Therapy and UGT1A1 Genotype” (A, with subsection links expanded).

The title links to the entire content of this record (B). In the record, the “In this Page” portlet on the right (insert, C) outlines its contents. All MGS summaries have similar organization, with sections that introduce the drug (or disease) and its relation to various genotypes. In this example, the record introduces irinotecan, a drug frequently used to treat metastatic colorectal cancer, and its association with a high incidence of toxicity. Patients carrying certain variants of the UGT1A1 gene are at an increased risk (D).

Separate sections of the record are dedicated to the drug overview, information about the gene, genetic testing and therapeutic recommendations based on genotype, and variant nomenclature (E).

The “Therapeutic Recommendations” section (F) summarizes recommendations from several sources, such as FDA and various working groups, and provides links to the complete recommendations for each of the sources (G).
MGS Use Cases (cont.)

Use Case 2: Correlate gene/allele nomenclature and access molecular data at NCBI.

Authors of research papers and other literature may use different symbols for the same gene and represent the same variant in various formats. Many of the MGS records provide tables that allow for matching genes’ symbols and/or allele nomenclature. In the same MGS record discussed in Use Case 1, the Nomenclature table (A) matches the common allele names with HGVS expressions and reference SNP identifiers from dbSNP, commonly referred to as the “rsID.” The MGS tables generally provide partial listings that include the most common alleles for a gene, but the links to comprehensive overviews are provided below the tables (B). Live links within the table connect clinicians to the clinical variants from ClinVar (C) and general variation record in dbSNP (D), which allow for further in-depth investigation of the variants.

Use Case 3: Find tests for HER2 gene overexpression in GTR.

The “Trastuzumab Therapy” record (E) states that trastuzumab is only used for treating breast cancers with “HER2 positive” tumors, in which the gene is overexpressed.

The overexpression of HER2 can be determined by immunohistochemistry (IHC), or testing for gene amplification using ISH/FISH assay (in situ hybridization/fluorescence in situ hybridization). The “Tests in GTR by Gene” (F) links to tests related to the ERBB2 (HER2) gene that were voluntarily deposited in GTR by test providers (laboratories). The left-side Filters allow for selections of relevant tests, with the example filtered by “Fluorescence in situ hybridization (FISH) (3)” (G).
MGS Use Cases (cont.)

Use Case 4: Use GTR as a portal to further investigate precision medicine-focused data.

In addition to tests/laboratory information, GTR also lists conditions that are associated with an individual gene. In the same GTR test set discussed in Use Case 3, click the “Genes” button (A) to retrieve the list of conditions.

The individual conditions (B) link to relevant records to provide aggregated information on these conditions. Here, the condition page for Trastuzumab response (C) displays the summary on the condition and provides links to other relevant resources (D), such as the corresponding record in MedGen (E). The “Recent clinical studies” section of the MedGen record lists recent publications on this subject, such as the entry on PTEN mutations (F) with its title linked to the abstract in PubMed (G). The right hand column (H) provides full-text links and links to similar articles for further exploration.