# UNG deficiency

## GENERAL INFORMATION

### Description:

Defects in UNG are a cause of immunodeficiency with hyper-IgM type 5 syndrome (HIGM5). Hyper-IgM syndrome is a condition characterized by normal or increased serum IgM concentrations associated with low or absent serum IgG, IgA, and IgE concentrations. HIGM5 is associated with profound impairment in immunoglobulin (Ig) class-switch recombination (CSR) at a DNA precleavage step.

### Alternative names:

- HIGM5
- Hyper-IgM syndrome 5
- Hyper-IgM syndrome, type 5
- Uracil-DNA glycolase

### Classification:

- Deficiencies predominantly affecting antibody production
  - Defects of class-switch recombination and somatic hypermutation (Hyper-IgM syndromes) affecting B cells

### Inheritance:

Autosomal recessive

### OMIM:

- #608106 Immunodeficiency with Hyper-IgM, type 5
- *191525 Uracil-DNA glycosylase, UNG

### Cross references:

**Phenotype related immunodeficiencies:**

- IDR factfile forX-linked hyper-IgM syndrome (CD40L deficiency)
- IDR factfile for non hyper-IgM syndrome
- IDR factfile for CD40 deficiency
- IDR factfile for X-linked hyper-IgM syndrome and hypohydrotic ectodermal dysplasia

### Incidence:

Incidence is not known.

## CLINICAL INFORMATION

### Description:

Symptoms are similar to those in XHIM syndrome, with increased risk of neutropenia, thrombocytopenia, hemolytic anemia, and gastrointestinal and liver involvement.
The clinical features associate a particular susceptibility to bacterial infections affecting essentially the upper respiratory tract and enlargement of secondary lymphoid organs, increased serum IgM concentrations, and profoundly decreased serum IgG and IgA concentrations.

### Diagnosis:

### Diagnostic laboratories:

**Clinical:**

- Molecular diagnosis of autosomal reccessive hyper-IgM syndrome, ORPHANET
- Hypogamaglobulinemia, eMedicine
- Pure B-cell disorder, eMedicine

## Therapeutic options:

- (Intravenous) immunoglobulins started early to achieve residual IgG level>8g/l. This treatment leads to a decreased number of infections and diminishes or normalizes IgM levels. The lymphoid hyperplasia is not influenced by treatment. In case of enlarged lymphadenopathies there is need for surgical resection or biopsy.
- Hypogamaglobulinemia, eMedicine
- Pure B-cell disorder, eMedicine

## Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies, coord. Edvart Smith

# GENE INFORMATION

## Names:

**HUGO name:** UNG
**Alias(es):** DGU, HIGM4, UDG, UNG1, UNG15, Uracil-DNA glycosylase, Uracil-DNA glycosylase 1, Uracil-DNA glycosylase

## Localization:

**Reference sequences:**

**DNA:** X15653 (EMBL) X89398 (EMBL) X89398 (EMBL) Y09008 (EMBL) AF526277 (EMBL) BC015205 (EMBL) BC050634 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** P13051 (SWISSPROT)

**Chromosomal Location:**

17q11.2

**Maps:**

UNG (Map View)

**Markers:**

RH15692, WI-19583

## Variations / Mutations:

- UNGbase; Mutation registry for UNG deficiency (Hyper-IgM syndrome, type 5)

## Other gene-based resources:

Ensembl: ENSG00000076248, GENATLAS: UNG, GeneCard: UNG, UniGene: 191334, Entrez Gene: 7374, euGenes: 7374, GDB: 119844, HomoloGene: 6585

# PROTEIN INFORMATION

## Description:

**Protein function:**

Excises uracil residues from the DNA which can arise as a result of misincorporation of dump residues by DNA polymerase or due to deamination of cytosine.

**Subunit:**

Monomer

**Subcellular location:**

Mitochondrial (isoform 1). Nuclear (isoform 2).

**Post-translational modification:**

Isoform 1 is processed by cleavage of a transit peptide.

**Tissue specificity:**

Isoform 1 is widely expressed with the highest expression in skeletal muscle, heart and testicles. Isoform 2 has the highest expression levels in tissues containing proliferating cells.

**Similarity:**

Belongs to the uracil-DNA glycosylase family.

## Structures (PDB):

| | |
|---|---|
| 1AKZ | Human Uracil-DNA Glycosylase |
| 1EMH | Crystal Structure Of Human Uracil-DNA Glycosylase Bound To Uncleaved Substrate-Containing DNA |
| 1EMJ | Uracil-DNA Glycosylase Bound To DNA Containing A 4'-Thio- 2'Deoxyuridine Analog Product |
| 1SSP | Wild-Type Uracil-DNA Glycosylase Bound To Uracil-Containing DNA |
| 1UGH | Crystal Structure Of Human Uracil-DNA Glycosylase In Complex With A Protein Inhibitor: Protein Mimicry Of DNA |
| 2SSP | Leucine-272-Alanine Uracil-DNA Glycosylase Bound To Abasic Site-Containing DNA |
| 4SKN | A Nucleotide-Flipping Mechanism From The Structure Of Human Uracil-DNA Glycosylase Bound To DNA |

## Other features:

**Other related resourses:**

PIR: A60472, InterPro: IPR003249; U_glycsylse_notp, InterPro: IPR002043; UDNA_glycsylse, InterPro: IPR005122; UDNA_glycsylseSF, Pfam: PF03167; UDG, ProDom: PD001589; U_glycsylse_notp, PROSITE: PS00130; U_DNA_GLYCOSYLASE

## Expression pattern for human:

| Tissue | Exp. (%) | Clones |
|---|---|---|
| germinal center B-cells | 8.26 | 1:585 |
| four pooled pituitary adenomas | 7.52 | 1:643 |
| stomach, adenocarcinoma | 4.78 | 1:1010 |
| four pooled high-grade tumors, including two primary tumors and two metastatic to ovary | 4.71 | 1:1025 |
| Burkitt lymphoma | 3.47 | 9:12544 |
| tumor | 2.65 | 4:7305 |
| 2 pooled high-grade transitional cell tumors | 2.64 | 2:3660 |
| fetal eyes | 2.60 | 2:3720 |
| adrenal cortex carcinoma, cell line | 2.34 | 3:6207 |
| germ cell tumor | 2.27 | 1:2133 |
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## Animal models:

**Mouse:**

MGD: ; Ung

## OTHER RESOURCES

# Societies:

**General:**

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies