Table 1: **Genes involved in primary HLH**

| **Gene** | **Protein** | **Function** |
|---|---|---|
| Genetic loci- 9$^{th}$ chromosome | Unknown | Unknown |
| PFR1 | Perforin | Cytolysis and immune regulation |
| UNC13D | MUNC13-4 | Prime cytolytic granules |
| STX11 | Syntaxin | Transport cytolytic granules |
| STXBP | Syntaxin binding protien | Fuse cytolytic granules to cell membrane, and release perforin |

Table 2: **Genetic abnormalities associated with HLH**

| **Condition** | **Gene affected** | **Function affected** | **Associated feature** |
|---|---|---|---|
| Griscelli | RAB27A | Uncontrolled T cell and macrophage activation; Defective docking | Albinism |
| Chediak Higashi | LYST | Defective biogenesis of cytolytic granules | Albinism |
| Hermansky Pudlak | AP3B1 | Defective transport of cytolytic granules | Albinism |
| X-linked lymphoproliferative disorder - 1 | SH2D1A, | Signaling lymphocytic activation molecule-associated protein (SAP) deficiency- inappropriate lymphocyte recruitment | Immunodeficiency Requires HSCT |
| X – linked lymphoproliferative disorder - 2 | BIRC4 | Inhibition of apoptosis | Immunodeficiency Uveitis (rare) Requires HSCT |

Table 3: **Biologicals and its Mechanism of action**

| **Biologicals used in HLH** | **Mechanism of action** | **Specially used in:** |
|---|---|---|
| Rituximab | CD 20 antibody | EBV associated HLH |
| Anakinra | IL-1 receptor antagonist | sJIA associated HLH |
| Alemtuzumab | CD 52 antibody | Serotherapy in HSCT for HLH |
| Tocilizumab | IL-6 receptor antagonist | Trials ongoing |
| Ruxolitinib | JAK 1,2, receptor antagonist | Trials ongoing |
| Emapalumab | IFN gamma antibody | Trials ongoing |
| Adalimumbab | TNF alpha inhibitor | Post-transplant associated HLH |

**Legends:**

Table 1: Genes involved in primary HLH

Table 2: Genetic abnormalities associated with HLH

Table 3: Biologicals and its Mechanism of action