Figure 6. Summary of molecules released from primary human hepatocytes exposed to test drugs and the impact of secreted molecules on hepatocytes and the immune system.

- ATP depletion
  - SMX-NO & Flucloxacillin ✓
  - Amoxicillin & Isoniazid X
- LDH release
  - SMX-NO & Flucloxacillin ✓
  - Amoxicillin & Isoniazid X
- Activation of Nrf2 marker genes
  - SMX-NO & Flucloxacillin ✓
  - Amoxicillin & Isoniazid X

**Cytokine secretion profile**

- **General stress profile**
  - (TNF-α, IL-1α, IL-1β, IL-6, IP-10,)

- **HMGB1 release**
  - (IFN-γ, IL-6, IL-10, IL-12, TNF-α)

- **Isoniazid-specific profile**
  - (IFN-γ, IL-10, IL-12, IL-17A)

- Activation of the adaptive immune response
- Direct killing of drug-stressed hepatocytes
- Polarisation of the adaptive immune response