

# Dissecting Drug-Induced-Liver-Injury

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## Research Questions

- ▶ How preclinical phenotypes translates to clinical adverse effects? How to identify the network of interactions between preclinical and clinical DILI-related endpoints?
- ▶ How to learn good latent representations of molecules?

## Assumptions

- ▶ Few hidden process that drive the whole toxicity landscape
- ▶ The association strength between  $s_i$  and  $s_j$  can be represented in term of similarity

## Method

- ▶ Matrix Factorization

$$\mathbf{E} = f_{\theta}(\mathbf{X})$$

$$\mathbf{D} = \mathbf{W}^T \mathbf{E} \quad \mathbf{S} = \mathbf{W}'^T \mathbf{Y}$$

$$\hat{\mathbf{A}} = \mathbf{D}^T \mathbf{S} + \mathbf{b}_n + \mathbf{b}_m$$

$$(\mathbf{A} - \hat{\mathbf{A}})^2 + \lambda_1 (\|\mathbf{S}\|^1) + \lambda_2 (\|\mathbf{D}\|^2)$$

- ▶ Classification loss (Binary cross Entropy)

$$\hat{a}_{ij} = \sigma(d_i^T s_j + b_i + b_j)$$

$$\min_{D, S} - \sum_{(i,j) \in A} \left( \underbrace{a_{ij} \log(\hat{a}_{ij}) + (1 - a_{ij}) \log(1 - \hat{a}_{ij})}_{\mathcal{L}_{BCE}} \right) + \lambda (\|d_i\|^2 + \|s_j\|^2)$$

$$\mathcal{L}_{BCE} = \sum_j \sum_i (a_{ij} \log \hat{a}_{ij} + (1 - a_{ij}) \log(1 - \hat{a}_{ij}))$$

- ▶ Pos-Negative weighting, Task weighting

$$\mathcal{L}_{BCE}^{wb} = \sum_j w_p \sum_i (w_p^+ a_{ij} \log \hat{a}_{ij} + (1 - a_{ij}) \log(1 - \hat{a}_{ij}))$$

$$w_p^+ = \alpha \frac{N_{p-}}{N_{p+}} + (1 - \alpha) 1$$

$$w_p = \beta \frac{N}{N_p} + (1 - \beta) 1$$

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## Figures

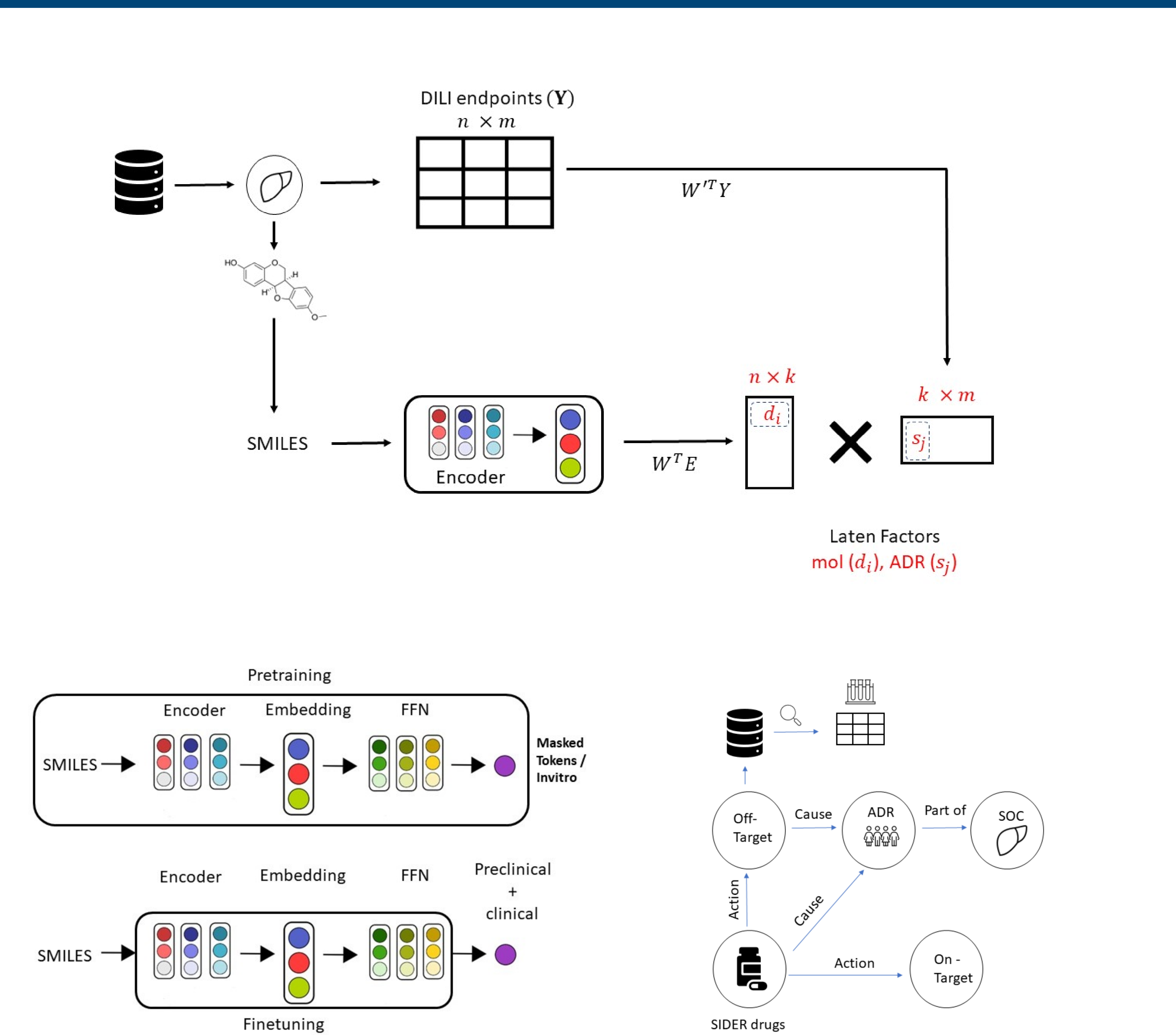


Fig. 2: Empowering encoder

Fig. 3: Ingestion of invitro data

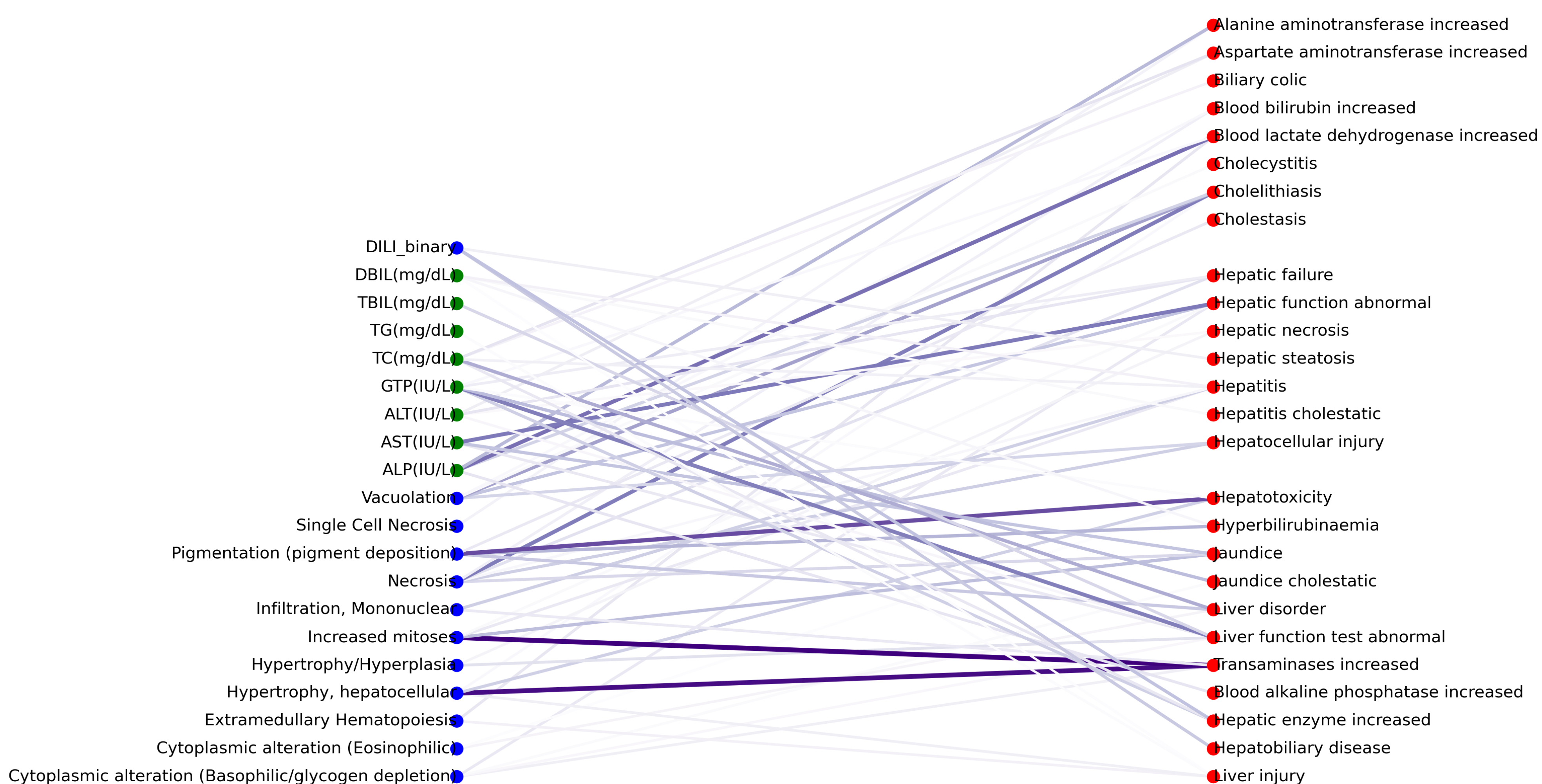


Fig. 4: DILI Network