Understanding chemotherapy-induced replicative stress to identify rational combination therapies

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Abstract
DNA damage-induced SSB to activating cancer signaling networks that include cell fate, cancer cell kill, DNA damage repair and survival (but also cell death). We have developed a multiscale computational model using the CDDGE environment to capture the Quintessential time points that chemotherapy-induced DNA damage repair signaling is in cell cycle. The computational model was trained and calibrated based on an extensive database that encapsulates cell cycle distribution of the initial cell population. The model was trained to include the most relevant and biologically plausible cell fate predictions. The model was then successfully used as a backbone for various new questions. Extensive simulations were performed to understand the outcomes of diverse therapies. The computational model, therefore, was used to understand the outcomes of diverse therapies. The outcomes were analyzed with the aim to identify rational combination therapies.

Construction of a multi-scale computational model to predict cell fate in response to chemotherapy

Identification of chemotherapy-potentiating drug combinations

\[ \text{DNA damage} \xrightarrow{\text{chemotherapy}} \text{cell death, DNA damage repair, survival (but also cell death)} \]

\[ \text{Computational model trained using the CDDGE environment to capture the Quintessential time points that chemotherapy-induced DNA damage repair signaling is in cell cycle.} \]

\[ \text{The computational model was trained and calibrated based on an extensive database that encapsulates cell cycle distribution of the initial cell population.} \]

\[ \text{The model was trained to include the most relevant and biologically plausible cell fate predictions.} \]

\[ \text{Extensive simulations were performed to understand the outcomes of diverse therapies.} \]

\[ \text{The computational model, therefore, was used to understand the outcomes of diverse therapies.} \]

\[ \text{The outcomes were analyzed with the aim to identify rational combination therapies.} \]

\[ \text{Figure 1: Illustration of the computational model describing the DNA damage response signaling, gene expression changes, cell cycle changes and cellular responses.} \]

\[ \text{Figure 2: Experimental datasets used to build the computational model.} \]

**A PASSION FOR OUTTHINKING CANCER**

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