Bridging multi-omic time series data and dynamic modelling

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1. Rationale

Introduction

- MicroRNAs (miRNAs) control over 60% of mammalian protein coding genes [1].
- Large time course mRNA and miRNA data sets may be generated more regularly.
- **Systems biology needs methods of integrating mRNA and miRNA data and locating specific mRNA-miRNA interactions for dynamic modelling. This is our aim.**
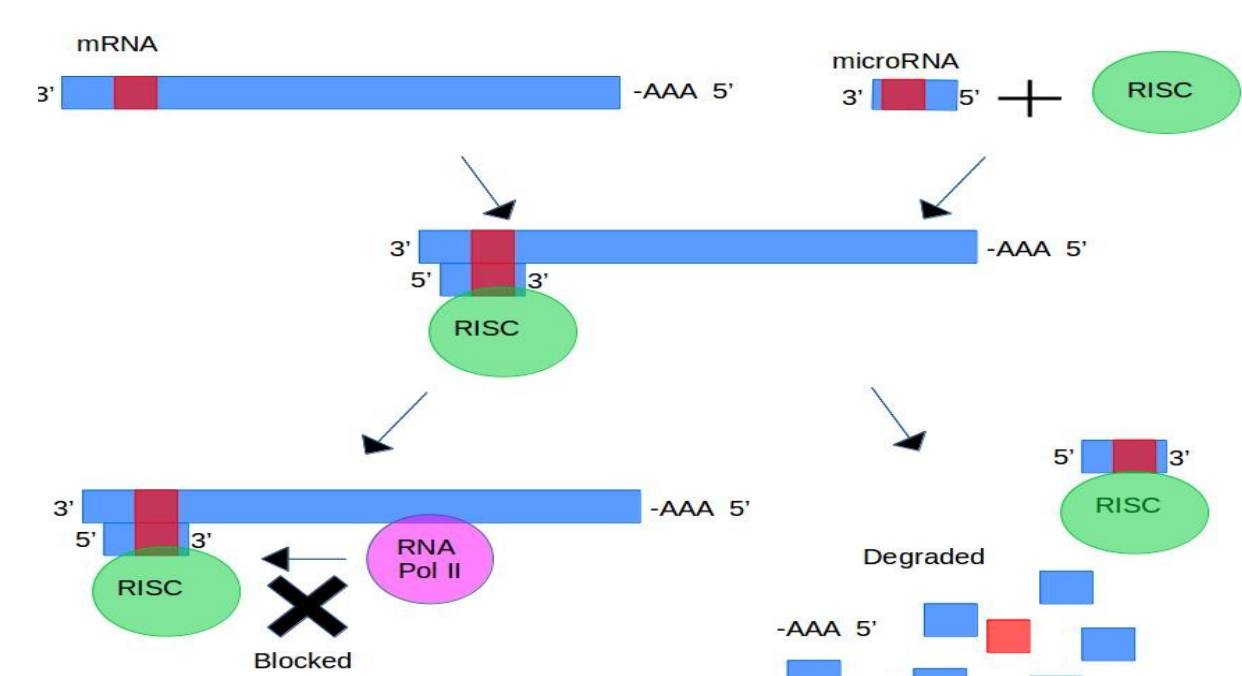

Fig. 1: Post-transcriptional modifications by mRNA-miRNA interactions

Methods

- Using various tools I have constructed a pipeline, inspired by previous methods [2].
- We used GSE47534 [3]. Here, mRNA and miRNA expression from MCF-7 cells were measured under normoxia and hypoxia.
- Measurements were taken at 0 hours/normoxia, and thereafter under hypoxic conditions at: 16, 32 and 48 hours.
- **This pipeline bridges big data bioinformatics and dynamic modelling.**
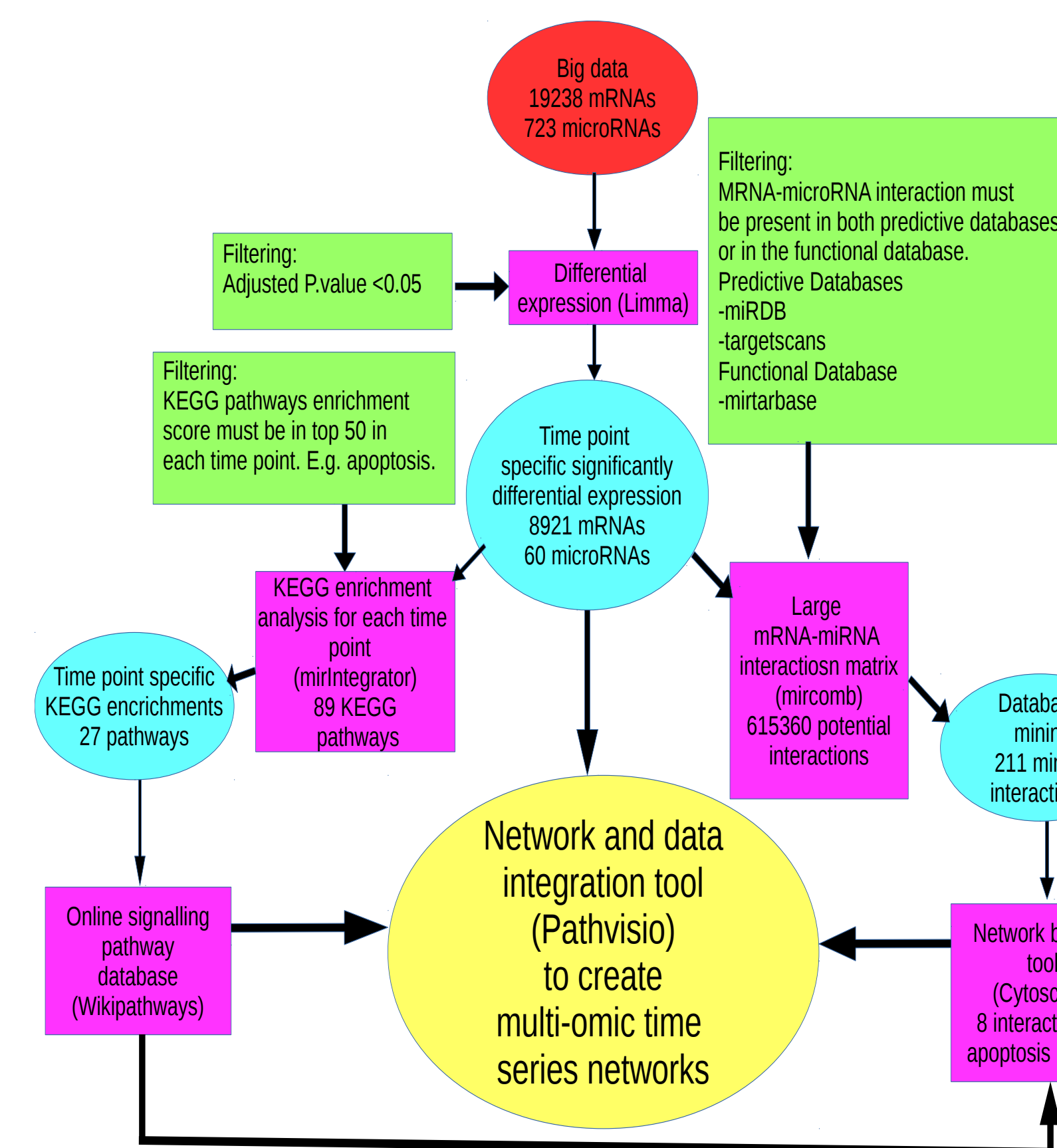
2. Pipeline

Figure 2 illustrates steps taken to reduce 19238 mRNAs and 723 miRNAs to 8 mRNA-miRNA interactions.

- Purple boxes = analysis which the different tools are performing. Tools are in the brackets [4–9].
- Blue circles = outcome of filtering.
- Green boxes = filtration.
- Red/yellow circle = input/output
- Ultimately, we create multi-omic time series networks which leads to gene regulatory networks and dynamic modelling, using CellDesigner and COPASI [10, 11].

Fig 2: Pipeline for creating multi-omic time series networks

3. Multi-omic time series networks

The networks below shows how a miRNA integrated apoptosis pathway changes in MCF-7 cells at 16, 32 and 48 hours under hypoxia. Colour changes represent log2FC differences between the respective time points and normoxic conditions (0 hours).
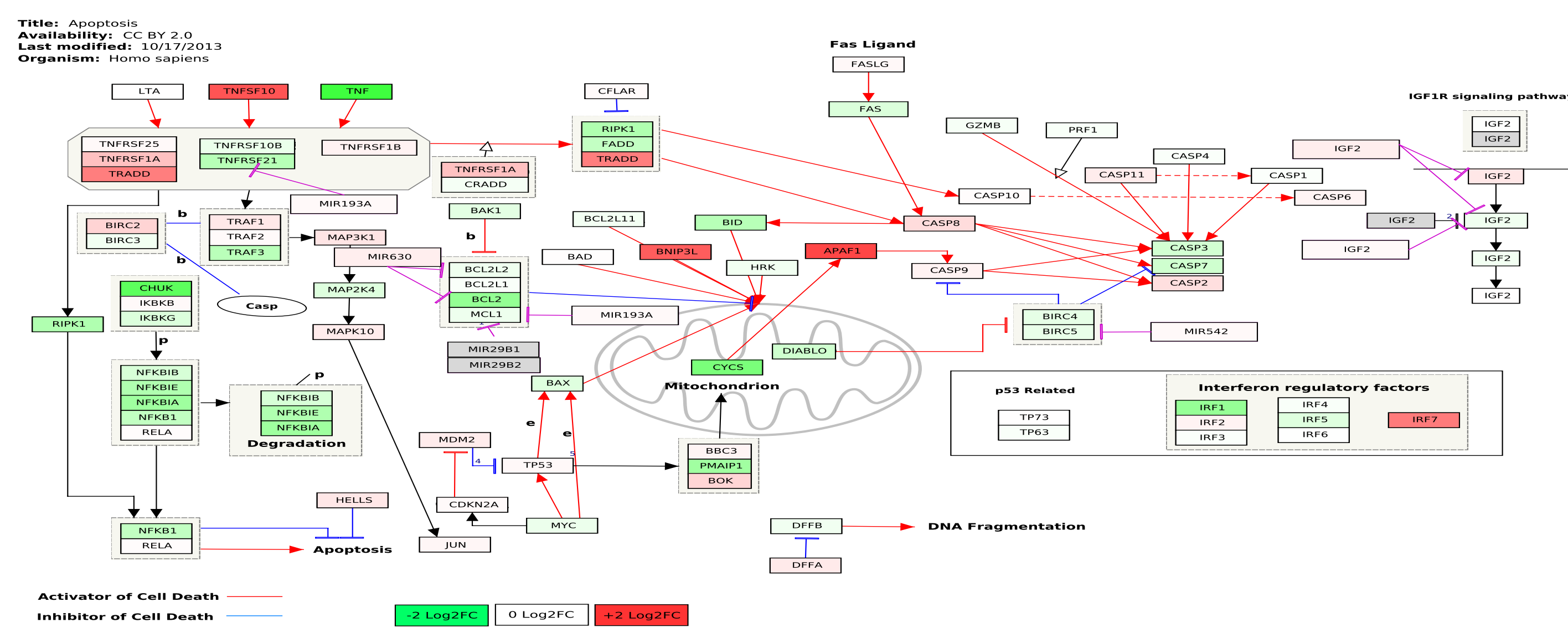

Fig. 3: Integrated mRNA-miRNA apoptosis pathway at 16 hours of Hypoxia
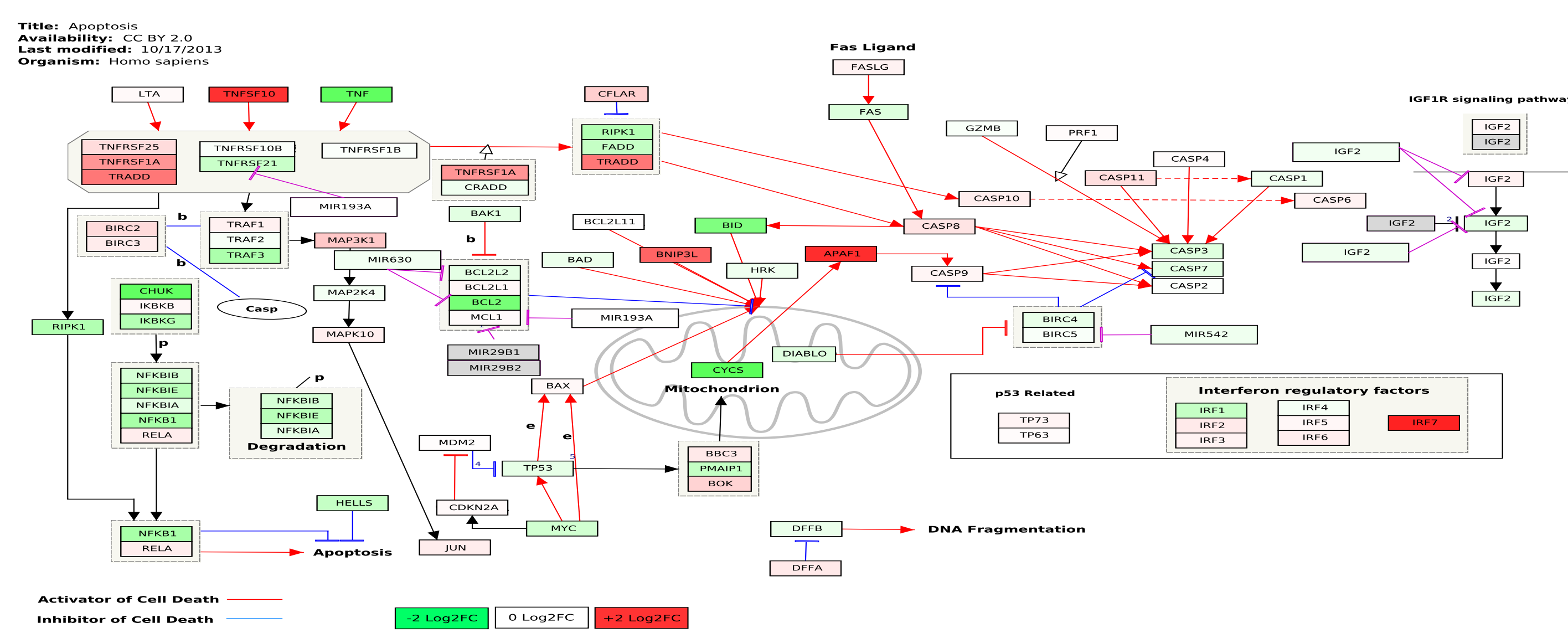

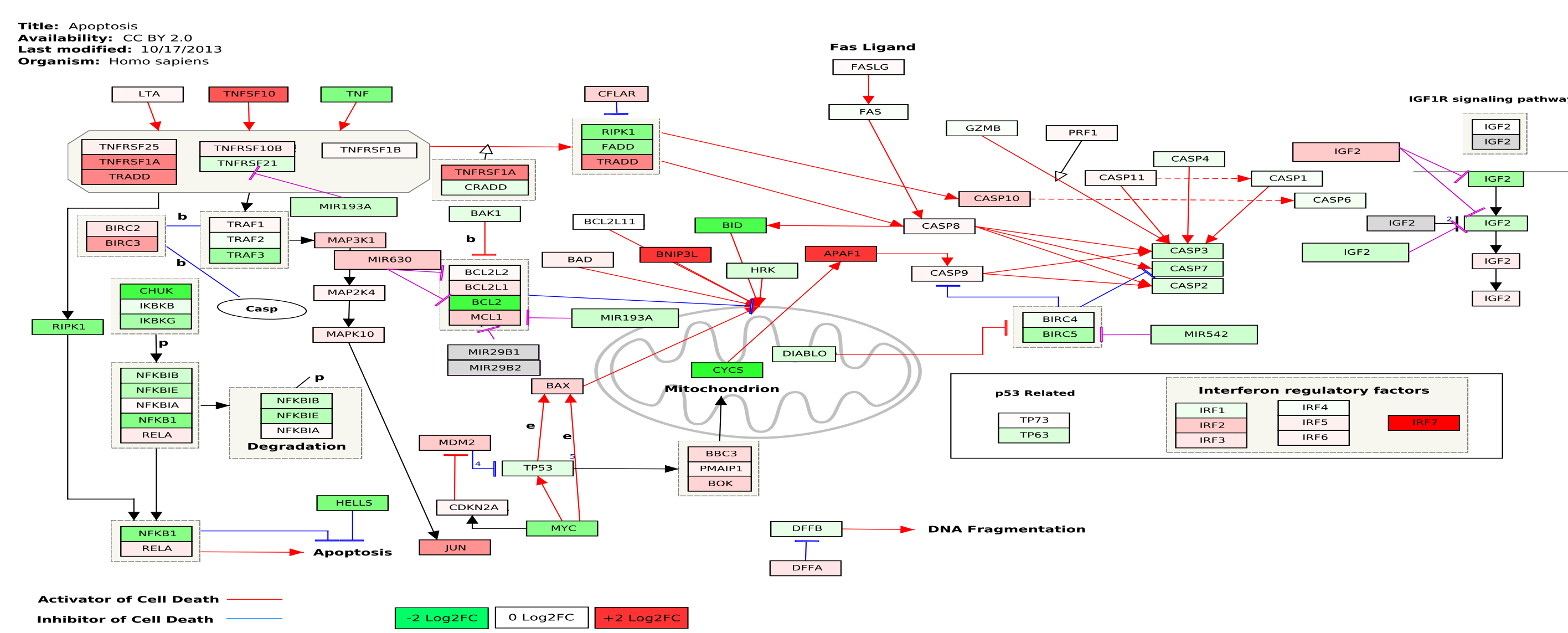Fig. 4: Integrated mRNA-miRNA apoptosis pathway at 32 hours of Hypoxia

Fig. 5: Integrated mRNA-miRNA apoptosis pathway at 48 hours of Hypoxia

4. Gene Regulatory Network

Fig. 6: Pipeline for multi 'omic time series network building

Species in Figure 6 were identified by the multi-omic time series pipeline used on the apoptosis pathway. Only transcriptomic data was available, so I chose to make a simpler RNA based model.

5. Dynamic mRNA-miRNA models

Fig. 7: Dynamic modelling of miR-mRNA interactions

Dynamic models in figure 7 indicate how MIR630 and MIR193a may regulate apoptosis under hypoxic conditions in breast cancer cells. Experimental evidence for BCL2-MIR630 and MCL1-MIR193a interactions is published [12, 13].

Concluding remarks

Conclusions

- **I have created a method to bridge the gap between multi-omic, time series data sets and dynamic modelling.**
- **Further investigation in both BCL2-MIR630 and MCL1-MIR193a may be fruitful in breast cancer research.**

References

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