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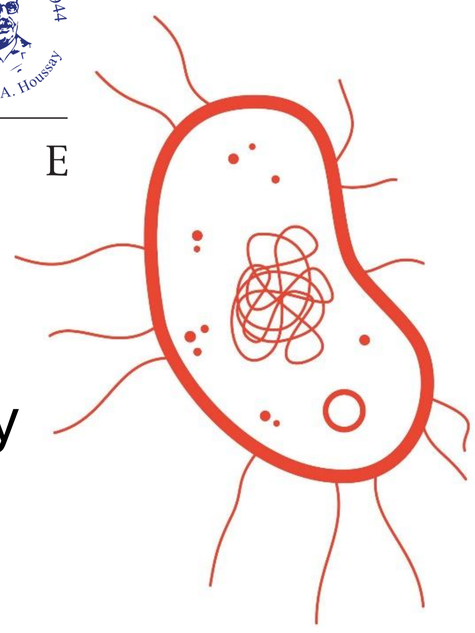

Integrated Genomic Analysis of Endometrial Cancer

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Bachelor's Thesis, Degree Programm in Bioanalytics and Cell Biology

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Expert: Dr., Philip Hoppe

INTRODUCTION

Endometrial Cancer

Type I
- higher hormonal sensitivity
- better prognosis

Type II
- hormone-independent
- worse prognosis [1], [2]

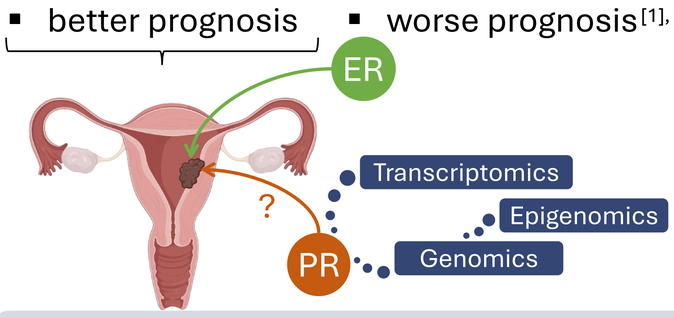

Fig. 1 Endometrial Cancer (EC) Type I. Estrogen receptor (ER) has been studied in endometrial cancer, while progesterone receptor (PR) remains underexplored and therefore is the focus of this study. [3], [4], [5]

Objective: integration of genomic, epi-genomic and transcriptomic data to identify regulatory drivers of type I endometrial cancer.

METHODS

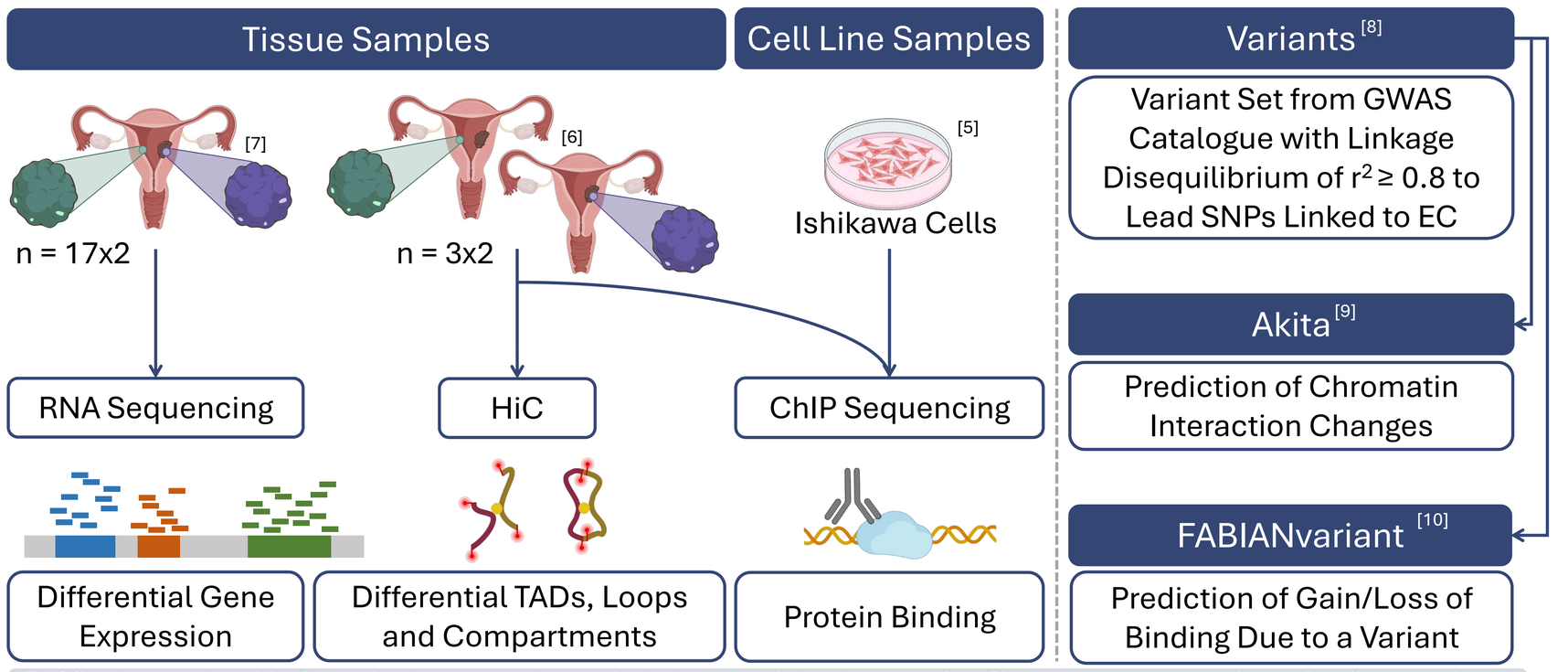

Fig. 2 Chart showing the origin of genomic data and key methodologies that were used in this study. Icons from Biorender.com and adapted images from Servier Medical Art (https://smart.servier.com/) were used, licensed under CC BY 4.0 (https://creativecommons.org/licenses/by/4.0/).

RESULTS

In total, 63 genes are associated with variants, PR binding and differential expression. They were ranked based on distance of those events to the nearest loop anchors.

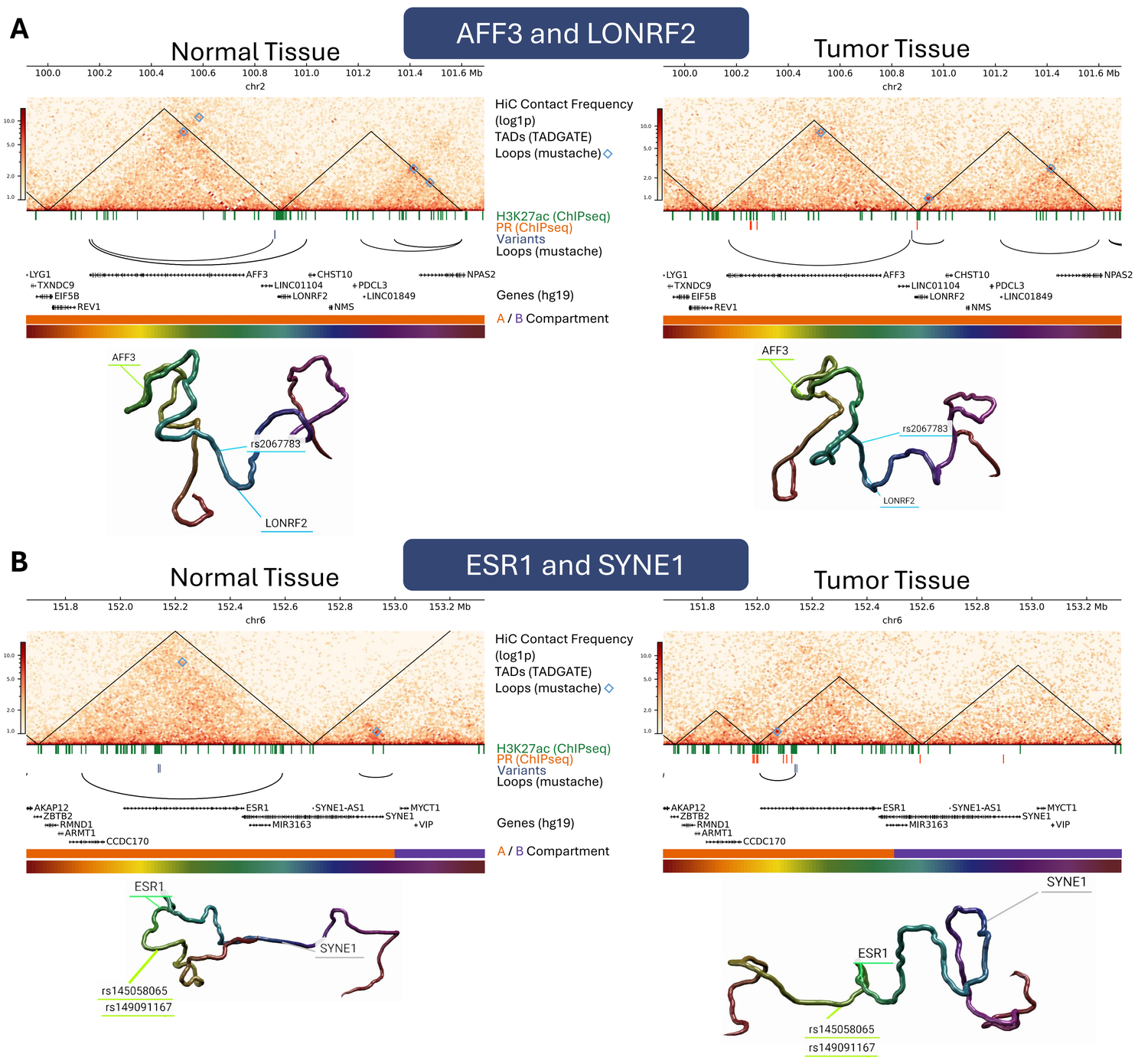

Fig. 3 Integrated genome view of the region containing the genes (**A**) AFF3 and LONRF2, and (**B**) ESR1 and SYNE1 comparing the topological landscape between normal endometrial tissue (left) and endometrial tumor tissue (right). Shown are HiC contact matrices (log1p) with annotated topologically associating domains (TADs), chromatin Loops, H3K27ac ChIPseq peaks, PR ChIPseq peaks, variants associated with a change in chromatin interaction, A/B compartmentalization and the corresponding 3D Model.

CONCLUSION

The two regions of AFF3 and LONRF2 as well as ESR1 and SYNE1 are associated with:
- topological differences
- differential gene expression
- PR binding
- variants leading to change in chromatin interactions

→ The causation of these events needs to be studied further.

Computational Analysis Shows Potential for Differential Transcription Factor Binding Sites (TFBS)

Future Directions

Correlation of Architechtural Protein Binding Sites with Gene Expression?

Gain / Loss of TFBS associated with Differential Gene Expression?

Driver Mutation?

Hotspot Region?

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The results shown here are in part based upon data generated by the TCGA Research Network: http://cancergenome.nih.gov/.