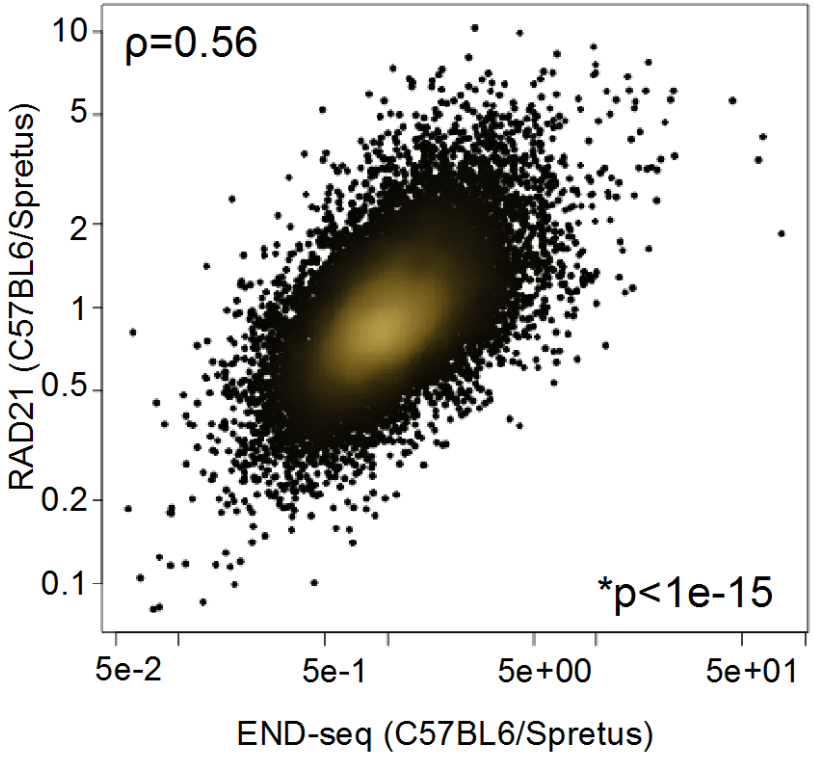
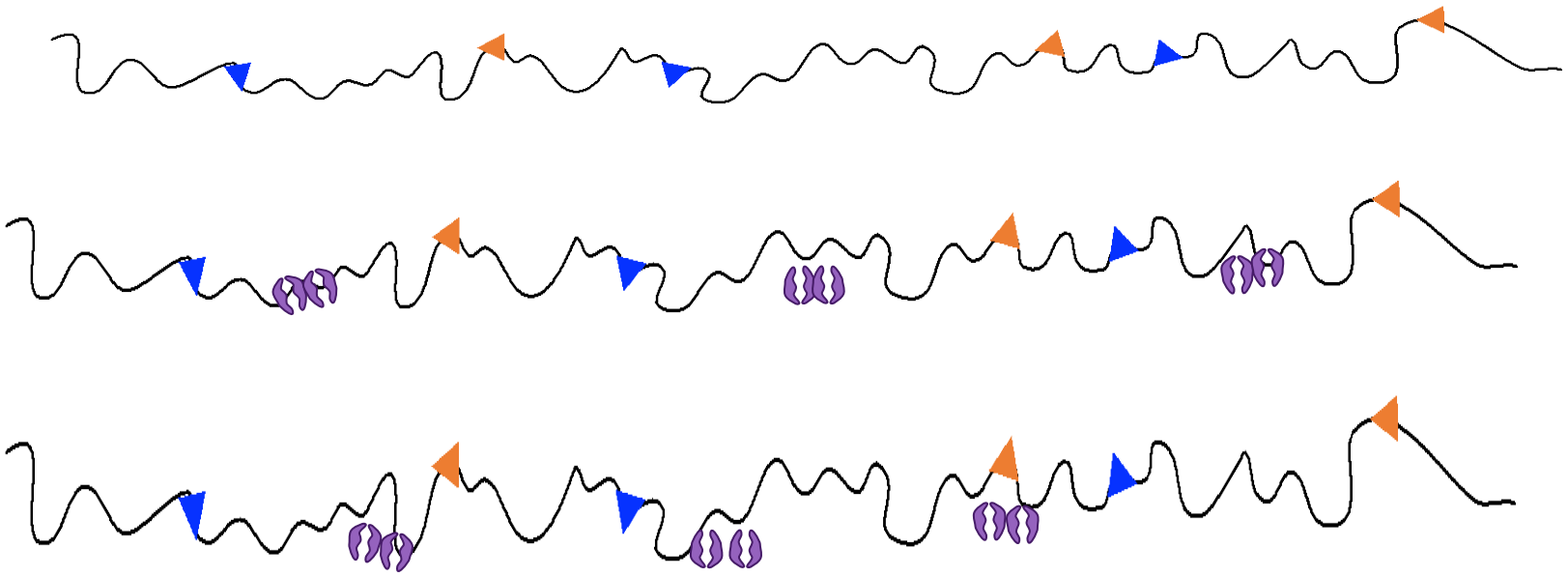
RAD21 binding at loop boundary predicts breakage frequency

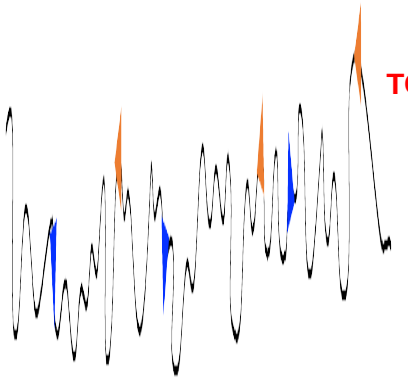


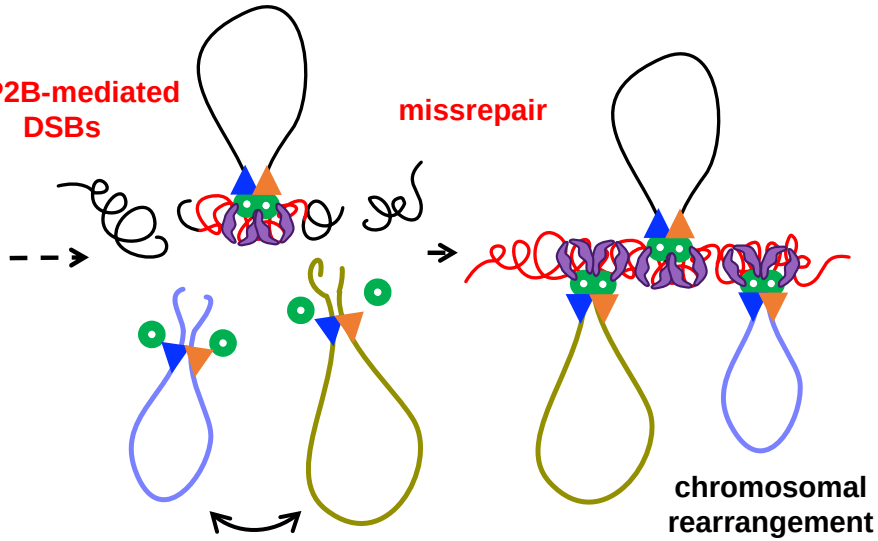
Conclusions

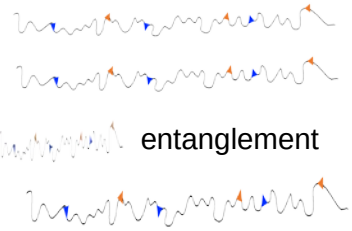
1. Many cancer fusion breakpoint cluster regions are direct targets of TOP2.
2. Oncogenic DSBs are conserved in different cell types (B-cells).
3. DSBs are dependent of TOP2B.
4. TOP2B DSBs are independent of transcription and replication.
5. DSBs are located 45nt outside chromatin loops bound CTCF/RAD21.
6. BCRs are localized at chromatin loop boundaries.
7. **Breakage frequency, TOP2 activity, is predicted by RAD21 (cohesin) binding.**

Torsional stress during loop formation makes chromosome loop anchors more vulnerable to TOP2 mediated DNA breaks.









Conclusions

1. **Many cancer fusion breakpoint cluster regions are direct targets of TOP2.**
2. **Oncogenic DSBs are conserved in different cell types (B-cells).**
3. **DSBs are dependent of TOP2B.**
4. **TOP2B DSBs are independent of transcription and replication.**
5. **DSBs are located 45nt outside chromatin loops bound CTCF/RAD21.**
6. **BCRs are localized at chromatin loop boundaries.**
7. **Breakage frequency is predicted by RAD21 (cohesin) binding.**
8. **TOP2B is always active at boundaries; thus torsional stress relief is continually needed, but could be dangerous.**

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