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# Different approaches to chromosome rearrangement detection in the model cell line

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*Motivation and Aim*: It is widely accepted that chromosome rearrangement can contribute to pathology and disease formation. However, the molecular underpinnings of the mechanism are not fully understood. Recent studies suggest that 3D genome organization is one of the factors at play [1], so to search for epigenetic consequences of chromosome rearrangements we have created a model cell line that allows to generate different combinations of rearrangements between 18 localized sites, with most of the rearrangements being in hemizygous state. For efficient use of this model system there is a strong demand for methods, allowing robust and scalable detection of the induced chromosome rearrangements. To achieve this, we devised two different approaches.
*Methods and Algorithms*: To induce a variety of chromosome rearrangements we genetically modified a near-haploid HAP1 cell line, introducing multiple LoxP-sites into the genome. We induced Cre-recombinase expression in the obtained cells for up to 20 weeks and collected them at different time points. Then we applied an inversePCR-based screening method that allows us to localize both ends of the rearrangement site [2] and thus detect rearrangements between different sites. Coverage was used to estimate the frequency of each rearrangement. We also modified this rearrangement detection strategy by performing digestion and ligation steps in fixed chromatin conditions similar to DNAse I Hi-C protocol [3].
*Results*: Both developed methods allowed us to detect rearrangements, with the second one being less biased and more consistent in replicas. According to our results, Cre-mediated recombination occurs much more often in *cis* than in *trans,* although several interchromsomal rearrangements were detected.
*Conclusion*: With a viable method to detect chromosome rearrangements in population screening we are able to choose optimal parameters of Cre-recombinase expression to generate a panel of subclones carrying different combinations of rearrangements. This work makes a step towards dissection of epigenetic changes accompanying different chromosome rearrangements.
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