

WHOLE GENOME SEQUENCING TO SURVEY GENETIC CHANGES IN STABLE CHO CELL LINES

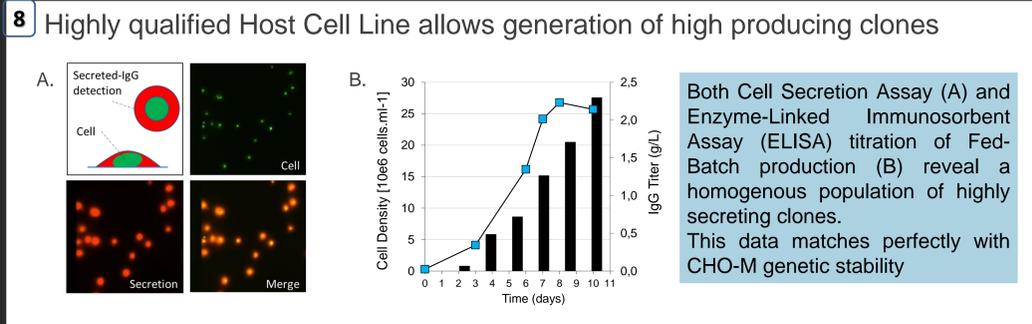
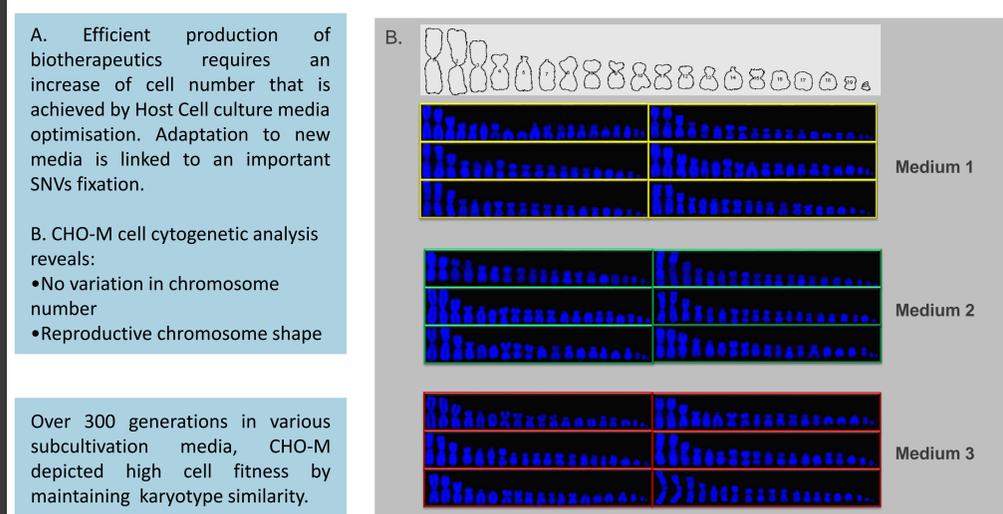
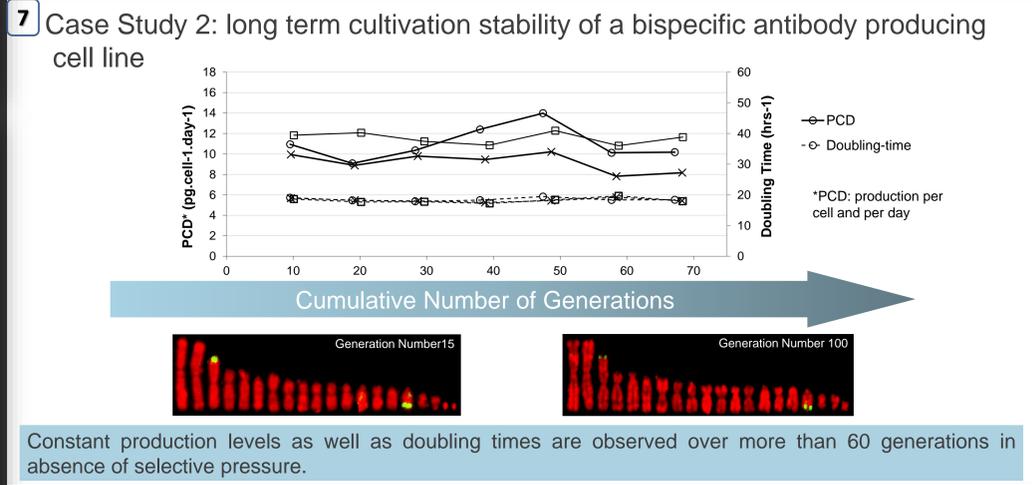
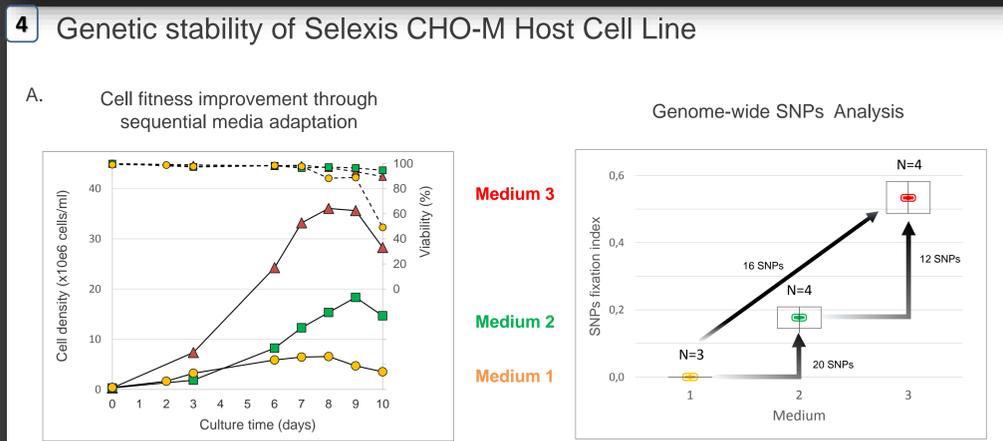
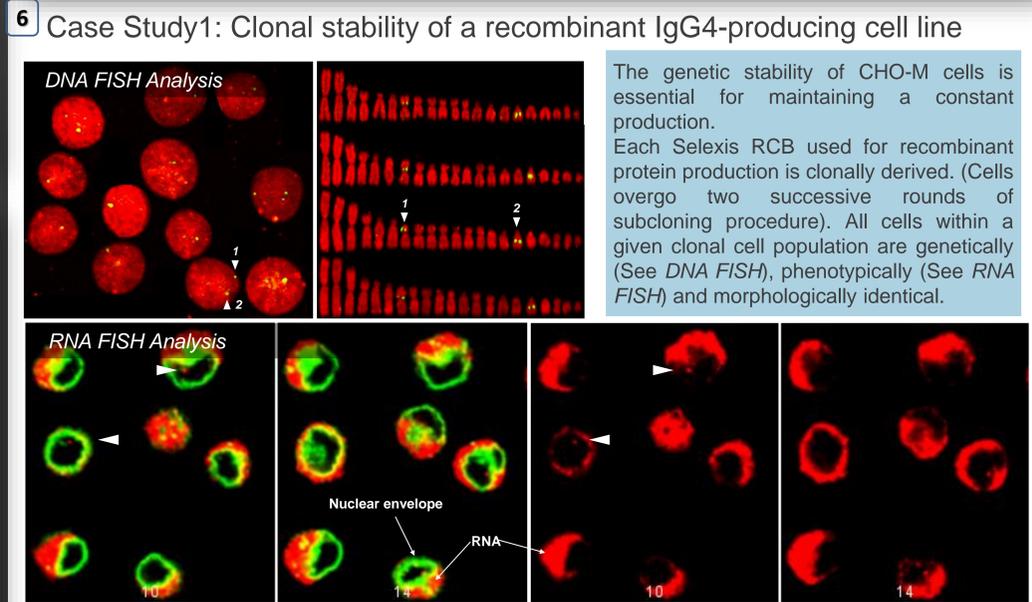
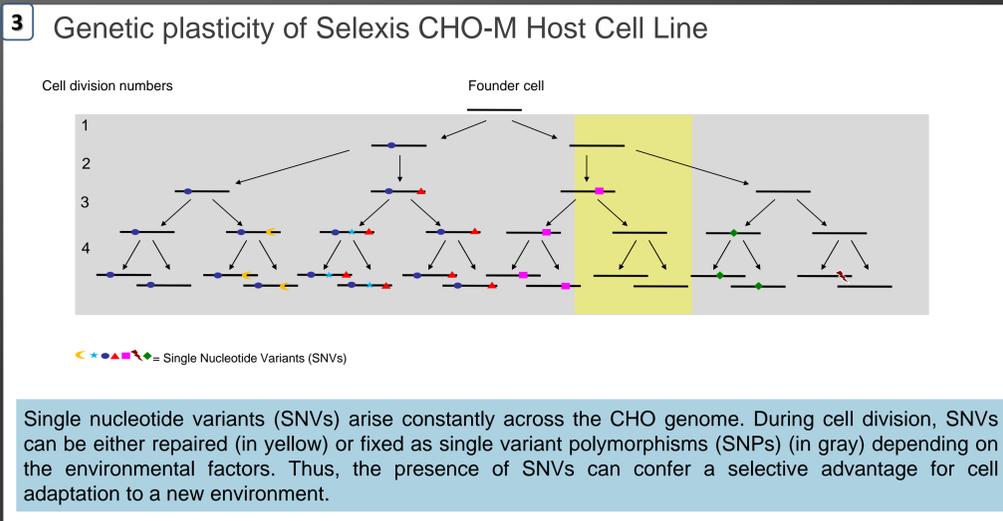
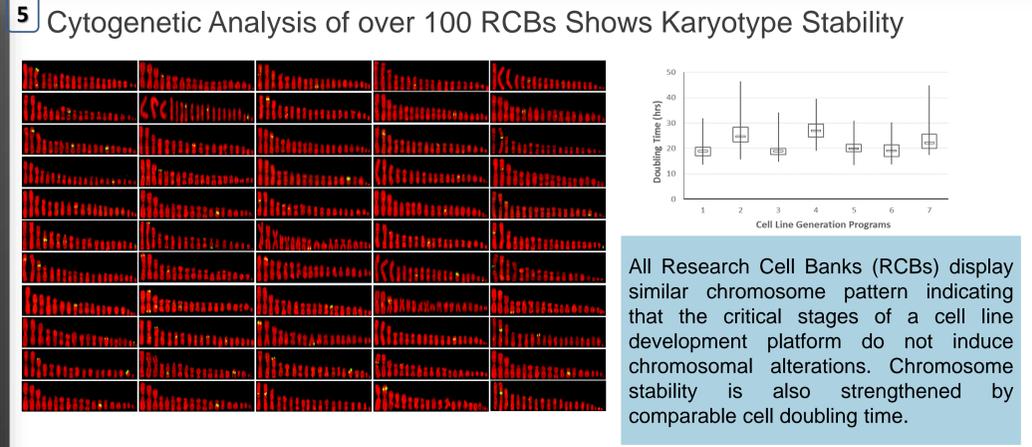
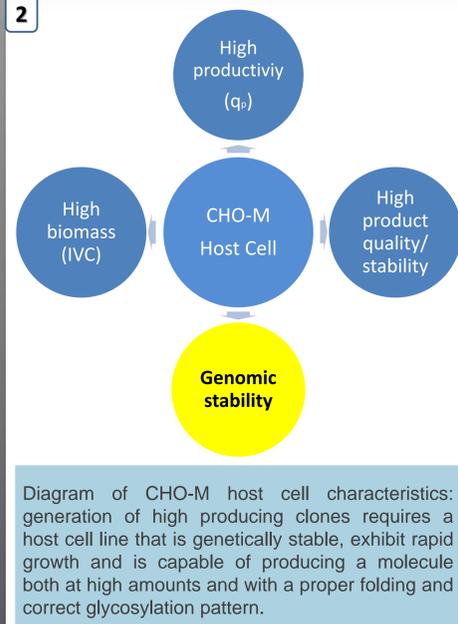
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1 Chinese hamster ovary (CHO) cells represent the most frequently applied host cell system for industrial manufacturing of recombinant protein therapeutics. Generating and identifying high producing clones in a fast and efficient way such that they do not lose their expression capability over time has been a major focus of the industry. Using cytogenetic analysis combined with Next-Generation Sequencing (NGS) technology and proprietary bioinformatic tools called SUREscan™, provide us with a unique ability to quickly analyze the whole genome of any generated cell line. Our data show that phenotypic changes in growth behavior and metabolism typically caused by cellular stress such as adaptation to a different media are associated with a rise in single nucleotide polymorphisms (SNPs). However, karyotype analysis of a large number of RCBs revealed that our CHO lineage is chromosomally stable indicating that the critical stages of a cell line production platform do not induce chromosomal changes. This contrasts with previous studies that have shown large chromosomal rearrangements in CHO cell lines [1, 2].



Conclusion

We found that phenotypic changes in growth behavior and metabolism that are typically caused by cellular stress such as adaptation to a different media are associated with a rise in single nucleotide polymorphisms (SNPs) detected using a single SNP regression approach. In light of the FDA and EMA recent concerns regarding establishment of clonality for IND and BLA submissions, these SNPs could be used to assess monoclonality. SUREscan™ can be used to improving traceability of RCBs, MCBs and WCBs. Singularly, karyotype analysis of over 100 RCBs revealed that our CHO lineage is chromosomally stable. Thus, none critical stage of the SUREtechnology Platform™ (transfection, selection and expansion) induce chromosomal changes.