

# Generation of pre-cursor of chemically expanded hepatocytes (pre-cHep)



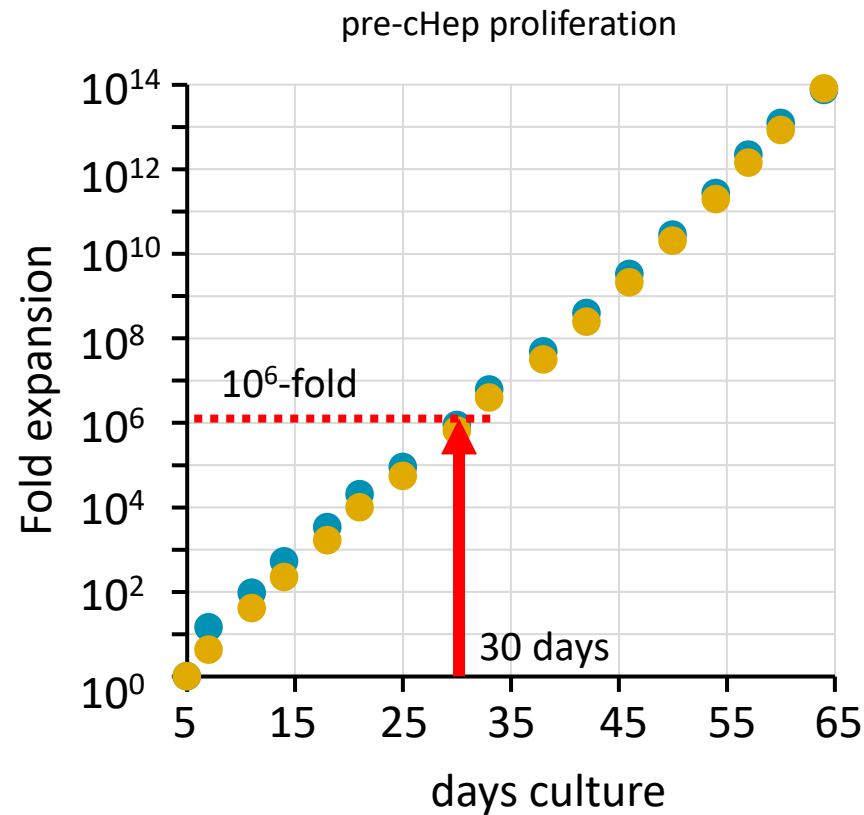
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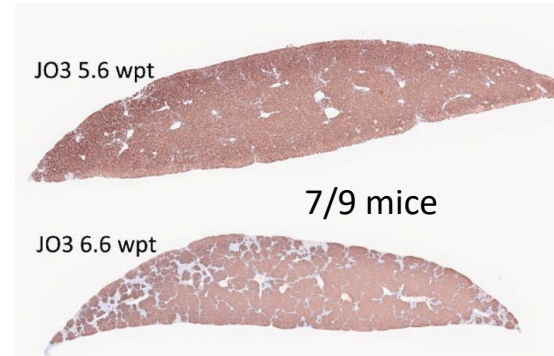
# pre-cHep can efficiently repopulate the liver

- The Kaji lab developed a culture condition that can reprogram primary human hepatocytes (PHH) into **pre**cursor of **c**hemically expanded **h**epatocytes (**pre-cHep**), which can expand  $>10^6$ -fold maintaining liver repopulation capacity within 30 days.

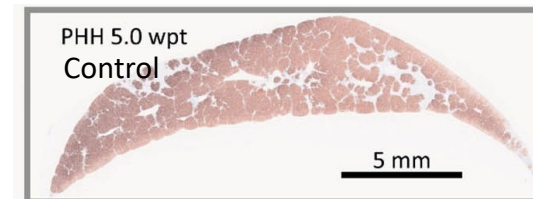
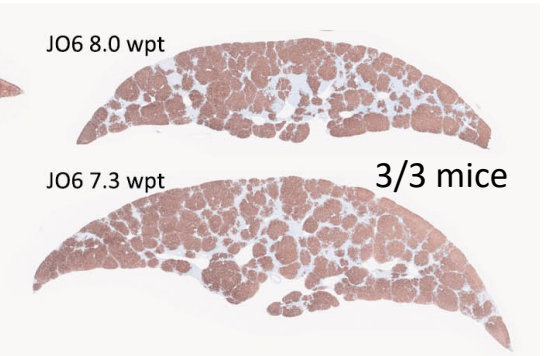


Injection in the liver of TK-NOG-hIL-6 mice  
by the Suemizu lab@CIEM

Day 30 JO3 pre-cHep injection



Day 30 JO6 pre-cHep injection



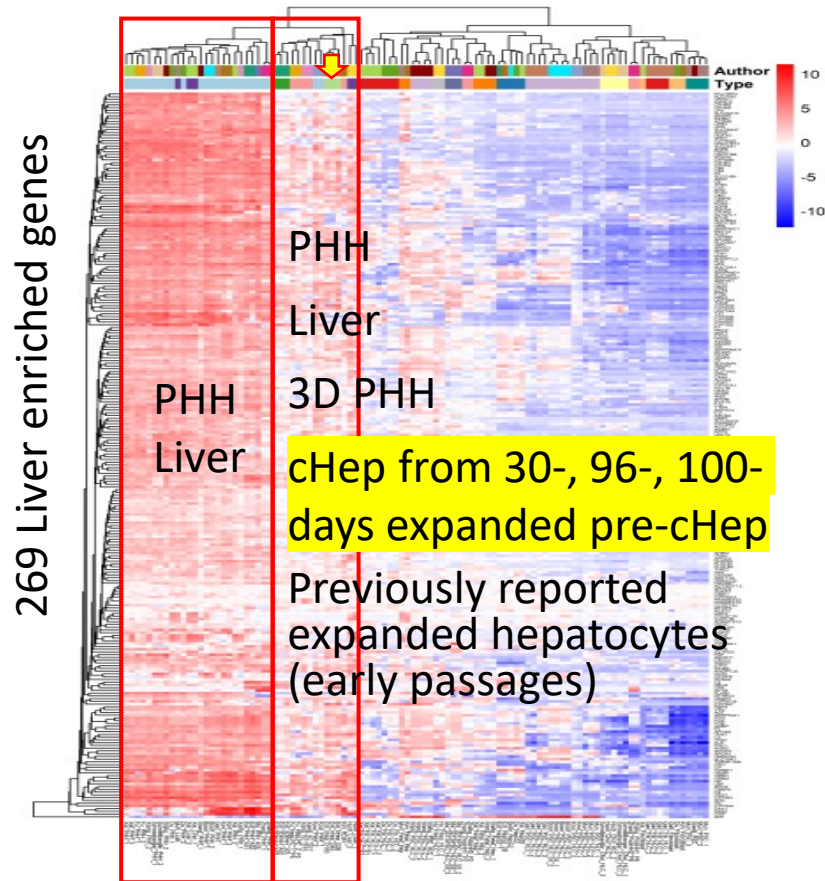
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# cHep have global gene expression similar to primary hepatocytes

- pre-cHep differentiate into chemically expanded hepatocytes (cHep) in 3-7 days *in vitro*.
- cHep have global gene expression similar to 3D cultured PHH, current gold standard in pharmaceutical companies, even after 100 days proliferation as pre-cHep, unlike other previously reported hepatocyte like cells.



## Summary

- ✓ 9 pre-cHep lines from 10 donors (2 months – 10 years old)
- ✓  $\sim 10^{12}$ -fold expansion in 60 days
- ✓ *In vitro* differentiation
- ✓ >80% liver repopulation till day 30 (2 of 2 tested lines)
- ✓ Genetically stable up to  $10^{12}$ -fold expansion (with SNP arrays, 2 of 2 lines)
- ✓ Toxicology testes underway in a pharmaceutical company
- ✓ Patent pending



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