pixlbio

CASE STUDY

Decoding biology.
Pixel by pixel.

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# pixlbio Wild-Type iPSC-derived hepatocyte models address population diversity

Population differences in drug efficacy and toxicity are a well-recognized challenge in drug discovery. These differences arise from a complex interplay of genetic, environmental, physiological, and behavioral factors that influence drug activity, metabolism, and clearance. Current models, however, fail to capture this variability: animal models assess efficacy and safety only within a single species, while in vitro liver models (e.g., primary human hepatocytes or hepatocellular carcinoma cell lines) are either limited in availability or derived from a single donor source. iPSC-derived cell models representing individuals of diverse ages, genders, and ethnicities can overcome these limitations, providing a robust platform to study how population diversity influences drug response early in development. At pixlbio, we hold a license to a diverse panel of wild-type donors, enabling the production of best-in-class iPSC-derived hepatocytes that address population heterogeneity.

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## pixHeps demonstrate the characteristic hepatocyte cobblestone morphology

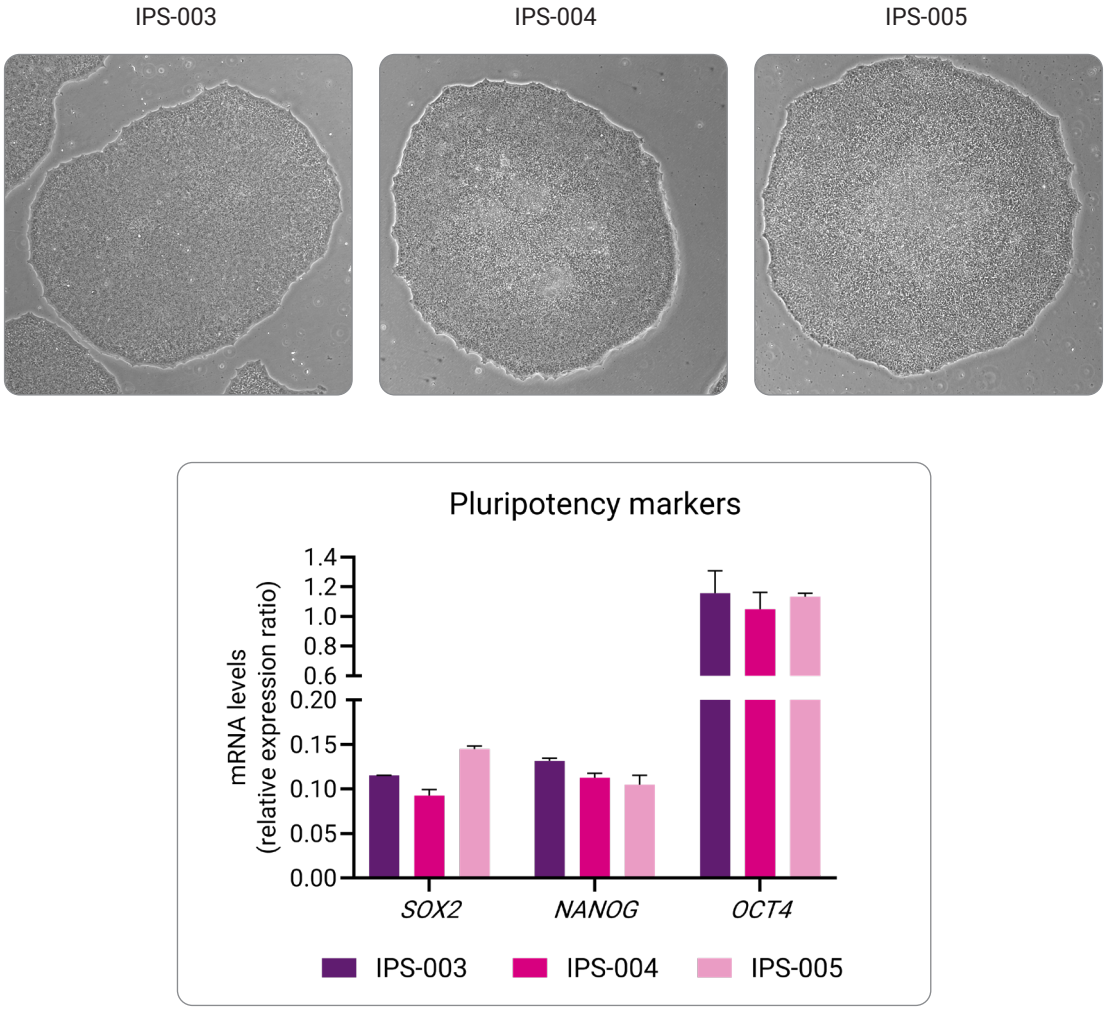


Figure 1: Representative brightfield pictures from pixlbio wild-type induced pluripotent stem cell lines (IPS-003: male donor, IPS-004: female donor, IPS-005: female donor) demonstrating compact and uniform iPSC colony morphology with defi ned edges and no evidence of spontaneous differentiation (upper). mRNA expression levels of the key pluripotency markers NANOG, SOX2, and OCT4 in pixlbio wild-type induced pluripotent stem cell lines (IPS-003, IPS-004, IPS-005) (bottom). mRNA data were normalized to GAPDH and are presented as mean±SEM of n=2 technical replicates.

## Wild-type pixHeps show similar morphology

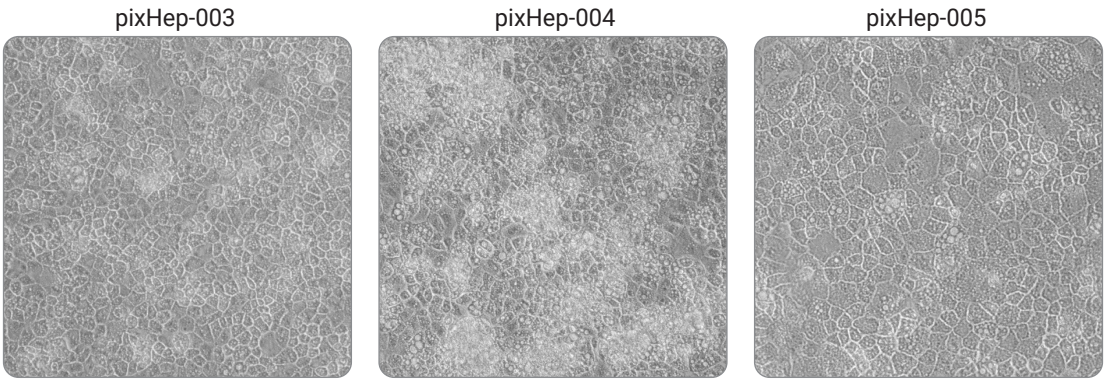


Figure 2: Representative brightfield pictures from pixlbio WT induced pluripotent stem cell-derived pixHeps (-003, -004,-005) demonstrating the characteristic cobblestone-like hepatocyte morphology.



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## Wild-type pixHeps show hepatocyte maturity

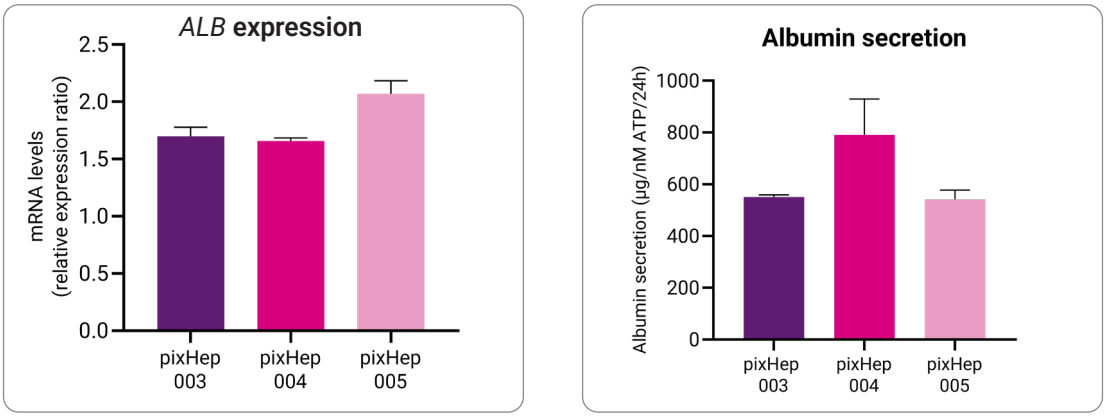


Figure 3: mRNA expression and secretion levels of the key hepatocyte maturity marker albumin (ALB) in pixlbio WT pixHeps (-003, -004, -005). RNA and secretion data were normalized to PPIA and ATP levels, respectively, and are presented as mean±SEM of n=1-3 biological replicates.

## Wild-type pixHep reveal differential CYP450 expression and activity

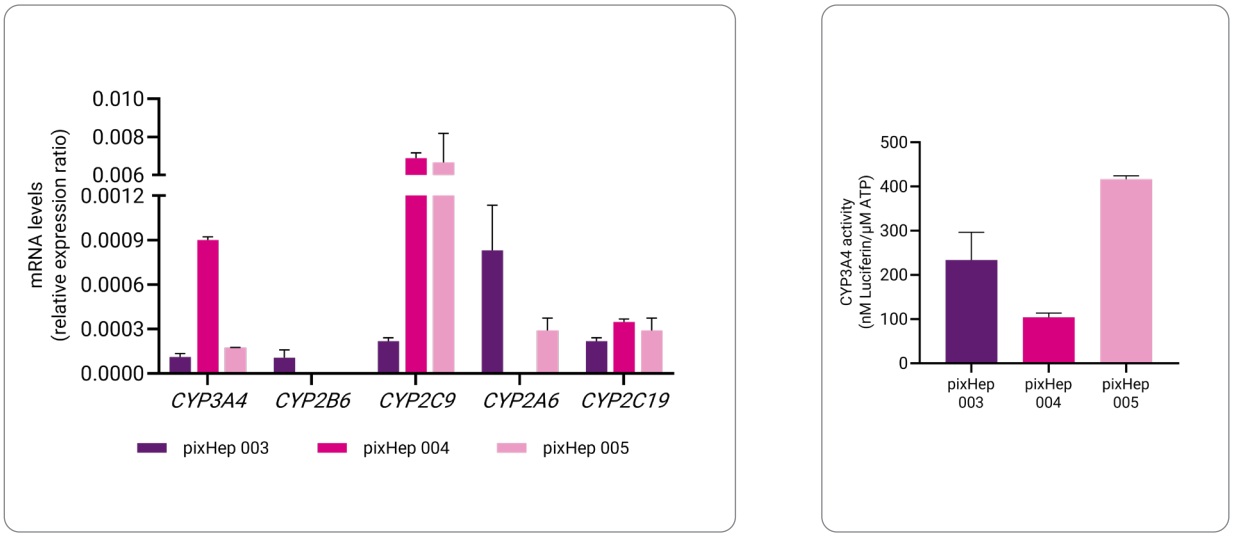


Figure 4: mRNA expression levels of Phase I CYP450 gene markers CYP3A4, CYP2B6, CYP2C9, CYP2A6, and CYP2C19 in wild-type pixHep (-003, -004, -005) (left). Basal CYP3A4 activity in wild-ty pixHep (-003, -004,-005) (right). mRNA and activity data were normalized to 18S rRNA and ATP levels, respectively, and are presented as mean±SEM of n=1-3 biological replicates.

### Conclusions

At pixlbio we successfully generate pixHep lines derived from multiple healthy individuals that capture donor-specific differences in CYP450 expression and activity. These data highlight the inter-individual variation observed in human population, giving scientists the opportunity to address variability in drug efficacy and toxicity screening early in drug development. Crucially, pixbio has access to a stem cell library consisting of  over 330 wild-type donors; leveraging this, we can expand our pixHep library with iPSCs derived from donors of different genetic and environmental backgrounds, offering, for the first time, an unlimited hepatocyte supply to identify adverse drug responses early, de-risk drug development, and ensure successful clinical outcomes.

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