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Universal lipid markers for early-stage embryos and microtissues

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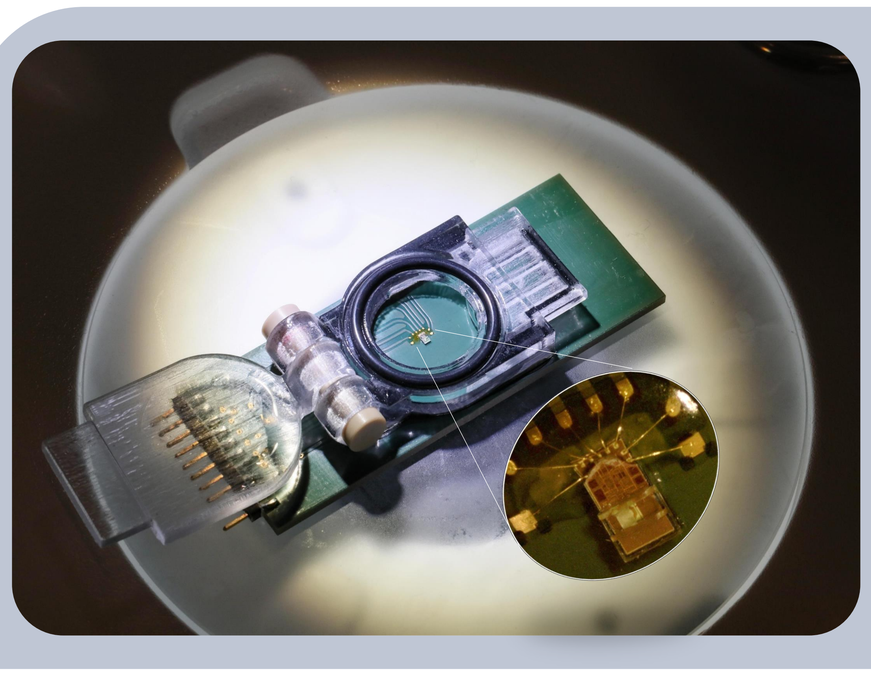
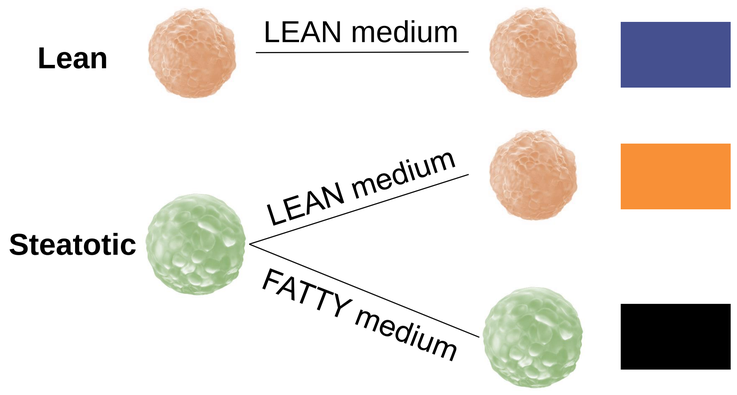


PROBLEM

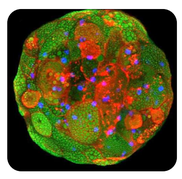
NMR is often referred as the golden standard for in-vivo studies of large organisms. Thanks to its unique resolving power and non-invasive nature, it is nowadays routinely applied to research and clinical investigations. These same investigations would be highly beneficial at the nanoliter scale (nL), typical of early development of mammalian embryos, organoids, and microtissues. Unfortunately, sensitivity and sample handling issues at such small scale (about 100 micrometers) prevented the adoption of NMR.

SOLUTION

Recently, our team has overcome these limitations with ultra-compact single-chip probes where microchip transceivers and 3D micro-printing are combined. It is demonstrated that such probes have sufficient sensitivity to resolve NMR signals from single human 3D cell cultures. **Right**: in human micro-livers we demonstrated high precision monitoring of fatty liver disease. The three groups are obtained by a control culture in lean medium (blue), a diabetic culture in diabetic medium (black), a diabetic culture exposed to lean medium (orange). Over time, the latter passes from disease to normal profile. The dynamics highlights that the recovery accelerates between Day 7 to Day 10 from exposure. These data originate from 117 measurements of single tissues.



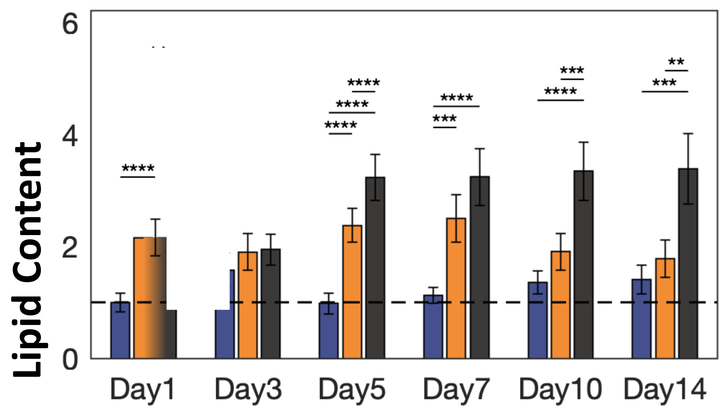
3D livers



Diameter
~ 220 µm

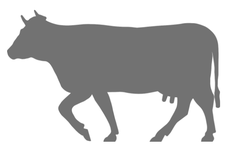
2020

Disease monitoring

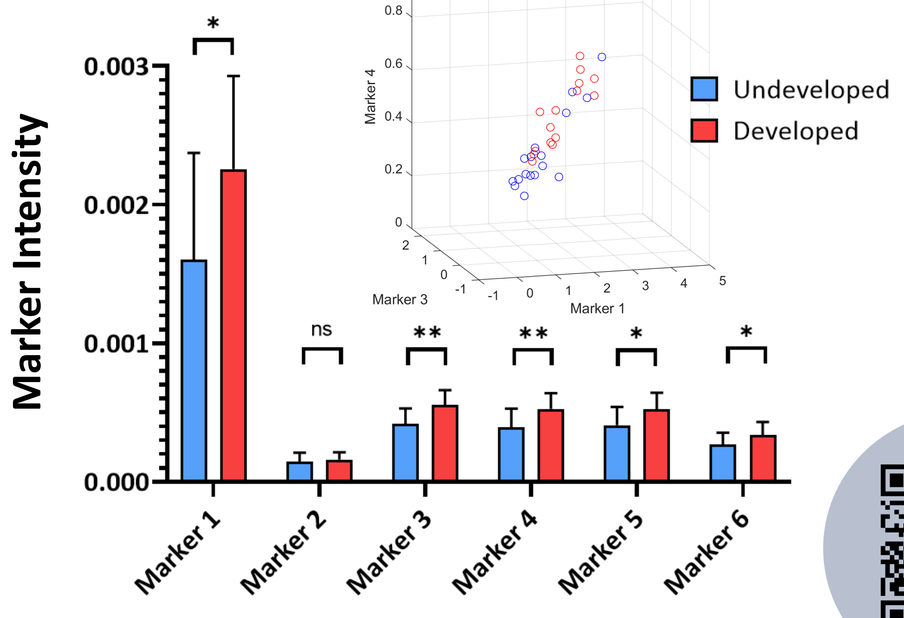


Lipid droplets
Regulating the cell's wellbeing

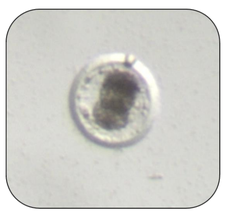
Bovine



Embryo development



2021



Diameter
~ 120 µm

BIOMARKERS

The dominant signals are largely originating from mobile lipids in droplets. Such features can be used to determine biomarkers, posing the basis for a novel non-invasive MRS-based microscopic screening tool for nanoliter cell cultures. **Left**: we observed similar lipid markers in early cow embryos divided in two groups: those arrested by 8-cell stage (Undeveloped) and those that continued to become blastocysts and morulae (Developed). Besides being able to separate the two groups, we have observed a significant spread in the "Developed" cohort. This is promising in the sense that variations between embryos reach 200%, so reflecting a much different balance of mobile lipids despite a similar morphology.

Partners

Keywords: Magnetic Resonance Spectroscopy, metabolism, embryo screening, non-invasive