Become a Founding Member of Ochre Bio's Organ ICU @ New York Biolabs (Hudson Square NYC)





www.linkedin.com/company/ochre-bio

BioEscalator, The Innovation Building, Oxford, OX3 7FZ, UK Taipei City, Nangang District, Yanjiuyuan Road, Section 1, **Taiwan** 180 Varick St Floor 6, New York, NY 10014, US

WHO WE ARE:

slides 2-6: Our Science slides 7-9: Our Team slides 10-11: Why Ochre Bio NYC

WHAT ROLES ARE AVAILABLE:

slides 12-13: Liver Cell & Molecular Biologists (Junior/Senior) slides 12-13: Liver Perfusion Associates

APPLYING FOR A ROLE:

slides 16-17: Next Steps slides 18-19: The Interviews

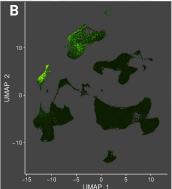






Taipei Lab (Discovery)

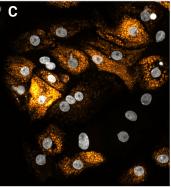


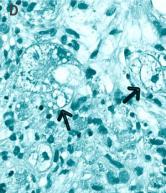


[A] Human liver biopsies in culture.

[B] Single-cell sequencing data showing the expression of an insulin signaling target in distinct cell types.

Oxford Lab (Validation)

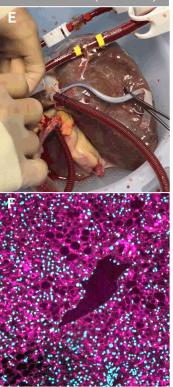




[C] Human microliver model accumulating fat (yellow).

[D] Human microliver model demonstrating ballooning degeneration (arrows).

Perfusion Labs (Preclinical)



[E] A perfused human liver at a UK perfusion lab.

[F] Imaging of a perfused liver, showing penetration of one of our liver-targeting RNAs (pink).

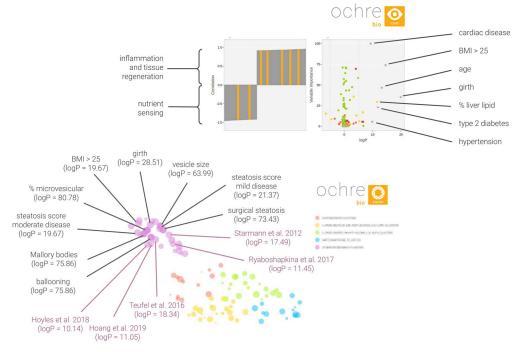
We Digitise Human Liver Biology At Scale

Deep phenotyping ('phenomics') is the combination of genetics, cellular genomics (single-cell and spatial sequencing), and advanced imaging to study each gene in specific cells in human tissues.

To do this at scale, we have built a global network of human liver labs. Our Taipei lab focuses on scaling our discovery efforts, using single-cell data from weekly liver biopsies. Our Oxford lab translates these discoveries, by validating our targets and optimising our therapies using human microliver models.

Then, at sites across the globe, we study the effects of our therapies in whole human livers kept alive on perfusion machines for days at a time.





[top] An example hit gene from 1000 donor livers, presented in Ochre Bio's software. To the left is the gene's hub of correlated/anticorrelated genes, presented a bars. The yellow bars are genes of particular interest, capturing two areas of biology associated with this gene: tissue regeneration and nutrient sensing. To the right are the gene's associations with donor clinical and histological phenotypes. The x-axis maps the log scaled p-values using marginal linear statistical models, while the y-axis maps how important each gene is in a multivariate nonlinear machine learner. Both indicate that the gene has an association with multiple cardiometabolic pathologies.

[bottom] An example of output from Ochre Bio's software, contextualising a phenotype from the 1000 donor livers (percentage lipid, assessed histologically) by comparing associated genes with other data sets. Each point represents a data set, with the purple cluster being most strongly associated with percentage lipid. Annotations in black are other internally generated data sets (their gene associations), while associations in purple are from published genes also associated with liver lipid accumulation.

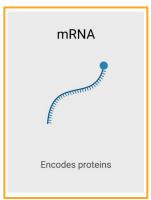
We Make Machine Learning Predictions

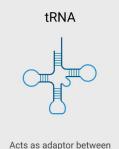
We generate data. A lot of it

Using machine learning, we automate processes, spot patterns, and make predictions about which genes could be good therapeutic targets. We like to think that we're working out how genes and cells talk to each other, and how this conversation changes with disease.

For more on our vision on building an actionable in silico liver, please view <u>one of our online</u> <u>webinars</u>.

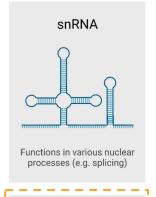
Types of RNA





mRNA and amino acids

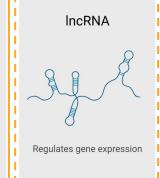












We currently focus on the therapeutic use of siRNA to silence overexpressed genes (by blocking mRNA). We chemically modify these siRNAs so that their effect lasts for many months, and conjugate a ligand so that the siRNAs target the desired cells.



We Turn Predictions Into RNA Therapies

2021 will be remembered as the year of RNA blockbusters. Not only RNA vaccines, but Novartis' Leqvio ®, a liver-specific long-acting RNA medicine that reduces blood cholesterol

Ochre Bio develops the same type of liver-specific long-acting RNA therapies. Once we are convinced that a gene's change in expression is causal, we optimise our synthetic siRNAs to knock down expression for months at a time in specific cell types.





Original Investigation | Gastroenterology and Hepatology

Trends in the Burden of Chronic Liver Disease Among Hospitalized US Adults

Grishma Hirode, MAS; Sammy Saab, MD, MPH; Robert J. Wong, MD, MS

The landscape of chronic liver disease (CLD) in the US is rapidly changing. This condition is currently the fourth leading cause of death among persons aged 45 to 64 years. With improvements in the management and treatment of viral hepatitis, the burden of liver disease is shifting toward alcoholic liver disease (ALD) and nonalcoholic fatty liver disease (NAFLD).

JAMA Network Open. 2020;3(4):e201997. doi:10.1001/jamanetworkopen.2020.1997

We Do This Because Transplant Waiting Lists are Growing

Chronic liver disease is the only top ten global kille that's on the rise. For more on this, see our health feature on Razor Science.

There are no cures for end-stage liver disease, except a transplant.

We are taking on liver disease by first focusing on improving the quality of donor livers. Why? One in four of us have chronic liver disease, meaning that transplant waiting lists are growing, while the quality of transplanted organs is decreasing.





Ouin is a medical doctor with further degrees in genetics, mathematics. computational biology, and a doctorate in systems genomics from Cambridge and Oxford Universities.

Quin started his first drug discovery liver genomics company over 15 years ago, with the emergence of functional genomics. Over the years he has held numerous leadership positions, from co-steering Oxford University's single-cell genomics consortium, to founding Novo Nordisk's Cellular and Systems Genomics Department.

Frustrated by the rising costs of healthcare in an ageing population, and the lack of therapeutic innovation in chronic liver diseases (a top 10 global cause of death). Ouin decided to start Ochre Bio with Jack.

Quin Wills MBBCh, BScHons, MPhil, MSc, DPhil Co-Founder, CSO

> Previous: Head of Cellular and Systems Genomics, Novo Nordisk





Jack O'Meara BEng. MSc Co-Founder, CEO

Previous: Helped see one of the first blockbuster gene therapies through regulatory approval

Jack is a biomedical engineer with an MSc in commercialising new technologies from the University of Notre Dame.

Prior to Ochre Bio, Jack was involved in founding and/or launching products for various biopharma and health technology companies, including the approval of Novartis' Zolgensma. His career spans management consulting, company creation, health technology and biopharma market launches.

Having always been fascinated by the intersection of healthcare, technology and business, Jack co-founded Ochre Bio with Quin to translate breakthroughs in transplant medicine and genomics, with a long-term vision in cardiometabolic healthspan.





Kenny Moore Head of Oxford Labs NASH Project Lead at Novo Nordisk: Lecturer at Oxford Uni



Allan Weber Head of Global **Transplant Programs** CEO of Essential Pharmaceuticals (acq Accord Healthcare)



Principal Scientist (X-Lab) Research Scientist,



Principal Scientist (X-Lab)

Postdoc at Max Planck Institute: Scientist at Harvard & MIT (contractor)



Head of Lead Development Head of Chemistry at the UK MRC Nucleic Acid Therapy Accelerator







Our Founders and Scientific Leadership





We Are a Growing Team

With over 35 team members, and counting, we are a scientific family with shared values around how we innovate - we live by Clarke's, Murphy's, and Wheaton's laws.













Ochre Bio NYC

If hypotheses are born in Taipei, refined (and therapeutics made) in Oxford, then they'll be tested in NYC.

In addition to our valued liver perfusion partners in the UK and US, we are setting up our own human liver perfusion lab in New York Biolabs. We're calling it our 'organ ICU' where the goal is to push the boundaries of how long we can keep human livers healthy on machines. Ochre Bio NYC won't be for everyone - we're looking for very determined scientists ready for long but rewarding days and nights maintaining and studying human livers.

NYC makes a natural next home for Ochre Bio, being close to Yale University, one of our perfusion partners. Ochre Bio NYC scientists will interact closely with our Yale colleagues.





Are you a total lab legend, looking to regenerate human livers by reprogramming them with advanced RNA therapies? Chronic liver disease is the only major global killer on a steep rise, with a significant unmet medical need. For many patients the only solution is a liver transplant.

Ochre Bio is a deep (genomic) phenotyping company, developing liver RNA therapies, testing them in human livers that we keep alive on machines for multiple days. We are expanding our current labs in Oxford (UK) and Taipei (Taiwan) to our third lab in downtown Manhattan (US). This new lab will be our 'Organ ICU' where we will routinely study perfused human livers, pushing the boundaries of organ repair.

We're looking for liver cell & molecular biologists (junior/senior) to deep phenotype all livers that we perfuse at our New York, Yale, and Oklahoma sites. That means: tissue imaging, blood and tissue functional studies, single-cell sequencing, and precision-slice culture of liver biopsies. You will be central to how we innovate around directly studying human liver biology over multiple days of perfusion (and in response to our therapies). There is ample scope to propose and work on side-projects with our Oxford and Taipei teams.

If this sounds like you, then please apply with a ~100 word cover note appended to your CV, highlighting three things that will impress us. Please clearly state if its a junior/senior role that you are seeking, together with your salary expectations. Successful applicants will be asked to a virtual chat before being invited to meet the broader team.

Salaries are highly competitive and dependent on experience. We are hiring at junior/senior scientist levels. We offer unique benefits, such as covering the costs of personal/professional development programmes that enable you to grow your scientific and soft skills. You'll be part of an international team, with ample opportunity for career growth. We sadly cannot sponsor visas, so ability to work in the US is essential.





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We are looking for full time or contractual perfusionists at our New York and/or Yale sites to help push the boundaries of liver perfusion with us. A typical shift will involve a 'patient' handover, monitoring the livers, problem solving and responding to poor liver metabolism, pH, lactate clearance and bile production. You will be trained up in performing biopsies, puncture haemostatic control, and flash freezing samples for study by the lab staff. There is ample scope to help shape and drive research programmes that will ultimately result in better quality donor livers

If you're looking for something a little different from your current clinical perfusion work, then apply with a ~100 word cover note appended to your CV, highlighting three things that will impress us. Please clearly state contractual availability and salary expectations. Successful applicants will be asked to a virtual chat before being invited to meet the broader team.

Salaries are highly competitive and dependent on experience. We are hiring at junior/senior levels. For full time employees, we offer unique benefits, such as covering the costs of personal/professional development programmes that enable you to grow your scientific and soft skills. You'll be part of an international team, with ample opportunity for career growth. We sadly cannot sponsor visas, so ability to work in the US is essential.





IT'S SIMPLE:

- Apply to <u>jobs@ochre-bio.com</u> with a ~100 word cover note appended to your CV, highlighting three things about you that will impress us.
- Please clearly state which role you're applying for.
- Please clearly state your salary expectations.





IT'S IN TWO PARTS:

- Successful applicants will first be invited to a 30 minute informal virtual chat. During this chat you will be given a chance to introduce yourself, and ask questions about the role and our science. We aim to provide feedback within 24h.
- Candidates who are further invited to a formal interview will do this at our New York Biolabs site where they will also virtually meet some of the Oxford senior team. Perfusion Associates will be asked to walk the team through their CV, followed by Q&A. Research applicants will be asked to give a 1 hour presentation that the Oxford team will virtually attend. The presentation will be: 20 minutes presentation on your scientific background, hard/soft skills you bring to the team, and one research project you're particularly proud of, 20 minutes presenting a technical problem, and then 20 minutes Q&A.