



Nucleome
THERAPEUTICS

Decoding genetics of the non-coding genome in inflammation

Dr. Mark Bodmer CEO
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Nucleome corporate overview

Oxford university spin out in 2019 of next generation 3D genomics technology

Series A \$50m in October 2022



Series B planned in 2025

Chair, CEO, CSO, appointed in past year

TECHNOLOGY

Differentiated scale and precision 3D genomics technology combined with AI/ML

SCIENCE

Emerging pipeline of genetically-discovered targets; First program in preclinical development

COMMERCIAL

Collaboration with J&J

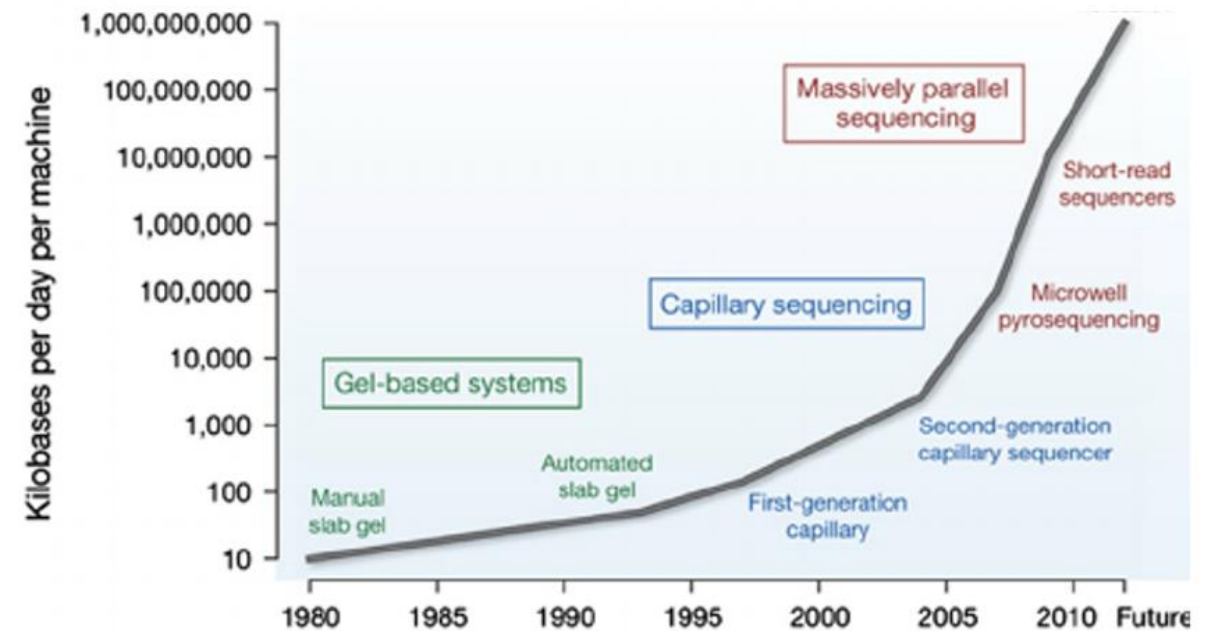
Nucleome's uniquely powerful genomics unleashes the potential of genetics

Millions of genetic variants (SNPs) are associated with thousands of diseases.

>95% of variants are in the non-coding genome with unknown function, regulating gene expression.

Non-coding human genetic variation holds the key to the molecular basis of disease.

Exponential growth in DNA sequencing capacity



Nucleome's lab + AI/ML technologies have the precision and scale to harness the potential of non-coding genetics for drug development.

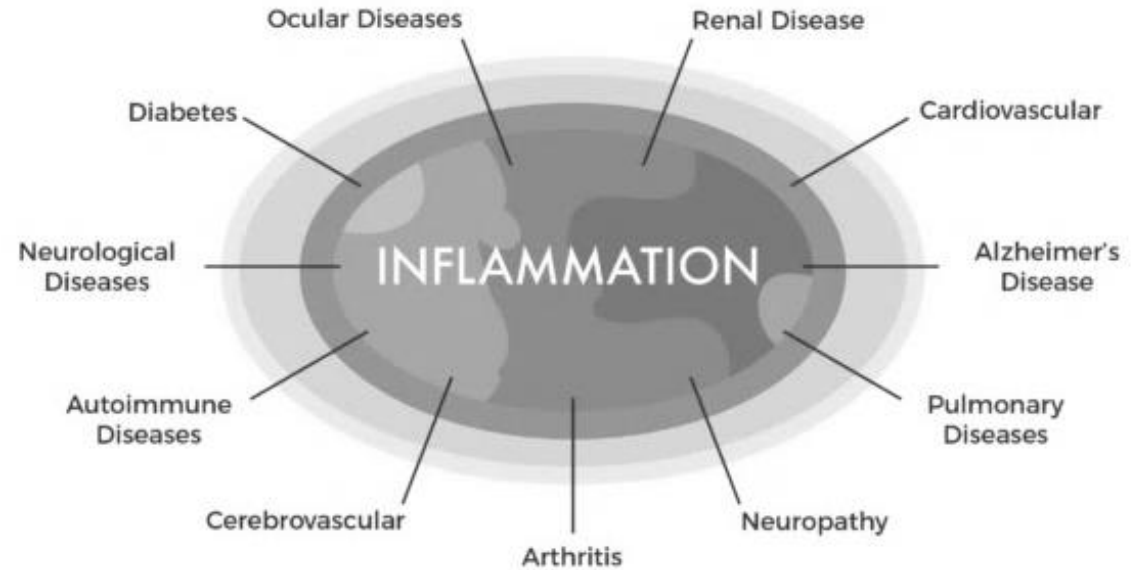
The impact of genetics on inflammatory diseases has yet to be revealed

Inflammation affects most diseases

Naturally-occurring human variants affect the regulation of **almost all genes of the immune system**

The immune system mediating inflammation is complex

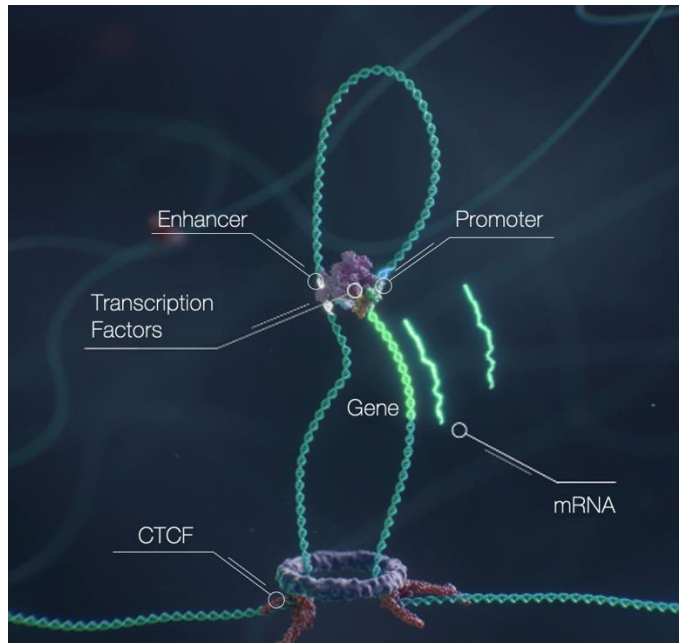
- Thousands of genes and SNPs
- Differential effects of SNPs in dozens of cell types



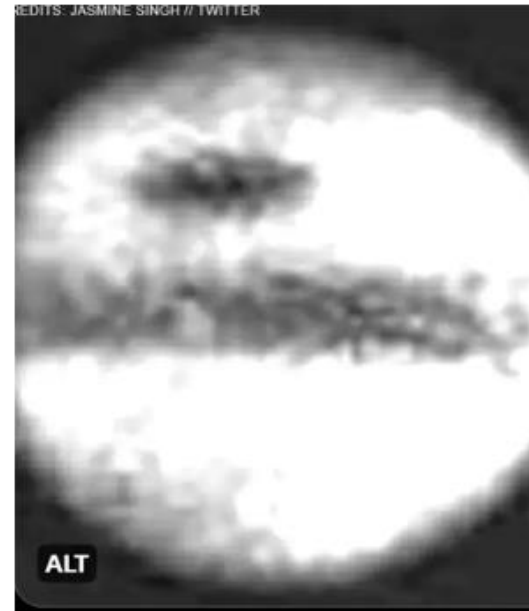
Nucleome's technology aligns functional **genetic variants** with **cell type** and **gene** to reveal molecular mechanisms of **inflammatory diseases**.

Micro Capture-C (MCC) is the James Webb Telescope of Regulatory Genomics

- Disease-associated variants are remote from their genes
- High resolution required to resolved gene regulatory networks



Promotor-capture Hi-C



Land-based telescope

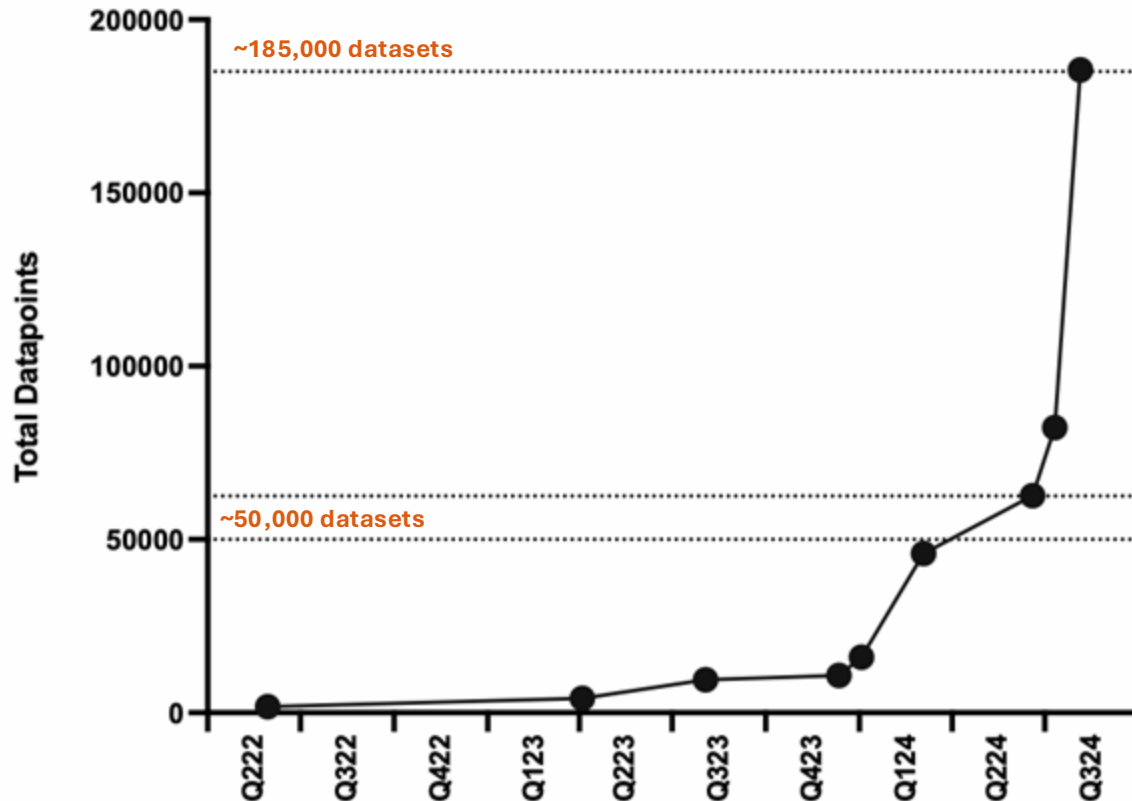
Micro Capture-C (MCC)



JWST

Nucleome has developed MCC to a transformational scale

Exponential and accurate growth of MCC

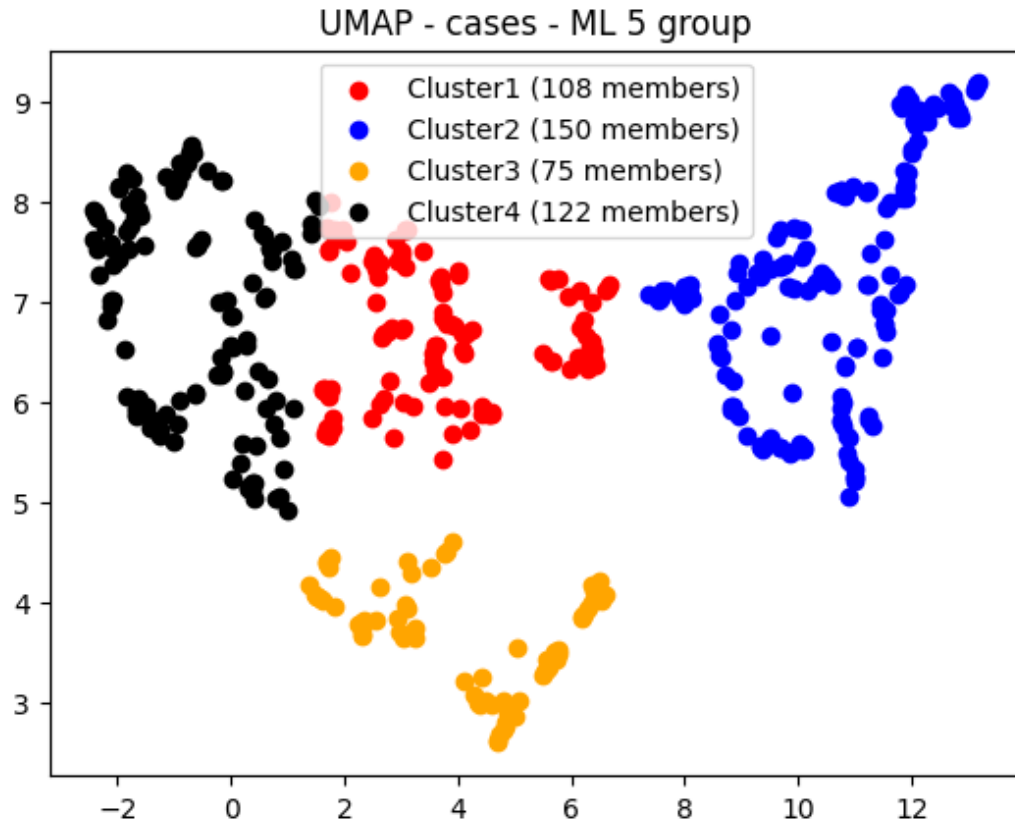


Scale is in two dimensions:

- Number of distinct cell types
- Number of enhancer/promoter pairs

3000 genes of druggable targets across **17 individual immune cell types** with multiple replicates

Beyond single loci: mechanistic map of RA from genetics



450 RA whole genomes form 4 non-overlapping endotypes

Nucleome aligns

- all regulatory genetic variants in a disease
– 2300 RA-associated SNPs
- 7 immune cell types
- all the genes they modify
- across genome sequences of 450 RA patients.

This reveals subtypes and molecular pathways of disease.

NTP464 target identified by genetic mapping in inflammation

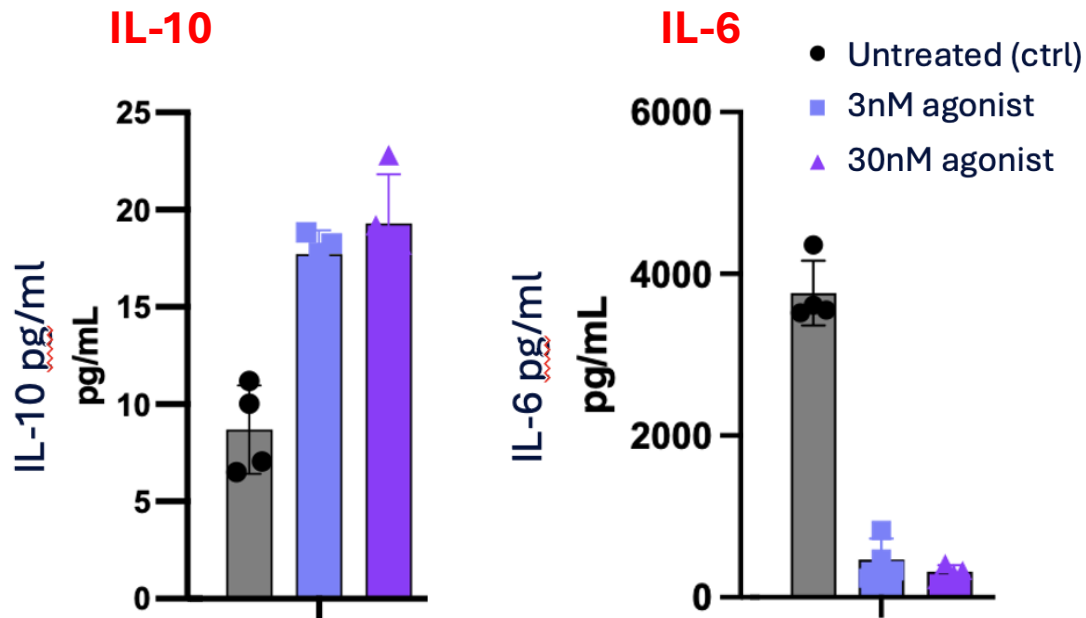
An emerging inflammation pipeline, including NTP464, has target ID, mechanistic mapping and potential patient ID.

Genetically-validated target in inflammation with likely broad application:

- SNP variant decreases activity of enhancer of target gene in activated immune cells – predicts agonism
- Tool agonist antibody identified in the literature:
- **First-in-class potential inflammation-resolving drug**, complementary to current SoC mechanisms
- **Development Candidate in 2025**

NTP464 tool has potent anti-inflammatory effects on primary human T cells

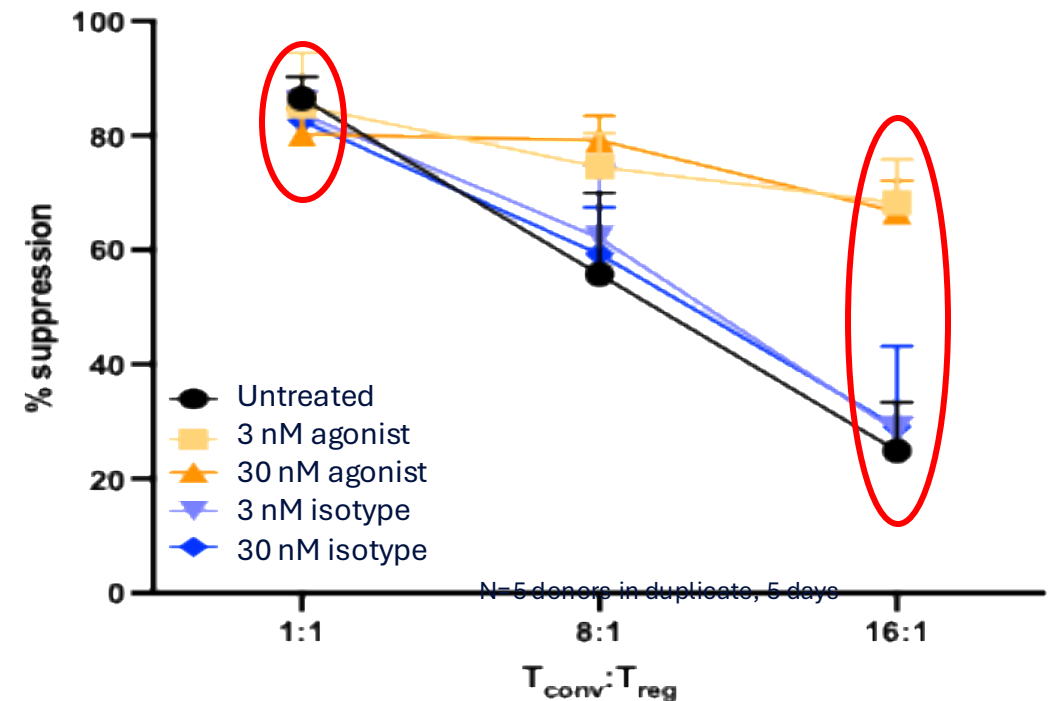
NTP464 tool compound elicits an anti-inflammatory state in Teff/Treg cells



- IL-10 increased
- IL-6 decreased substantially

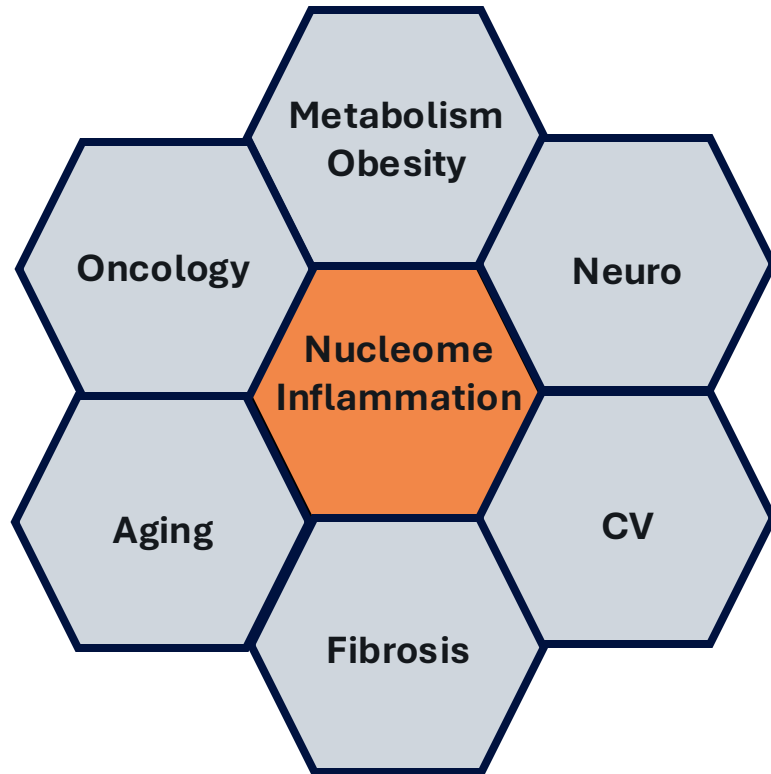
The effect was on function and not cell number

Enhancement of suppression by Tregs



Dose-dependent effect of the agonist is the equivalent of **quadrupling Tregs**.

Inflammatory diseases depth is a template for TA breadth



Nucleome's investment in non-coding genetics of inflammation has created a modular model to apply in other therapeutic areas.



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The **unparalleled precision** of Nucleome's technology for the first time harnesses non-coding genetics for drug development