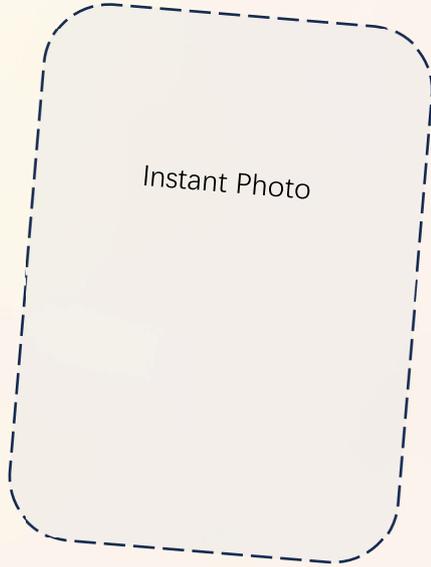




# IDEA

International  
Directed Evolution  
Competition  
2023







## FRIENDSHIP STAMP

This is the Wall of iDEC Friendship!

**Instant photos:** Everyone can have one free snapshot (£5 Donation for the second), and you can invite our volunteers to take the photo for you and your friends.

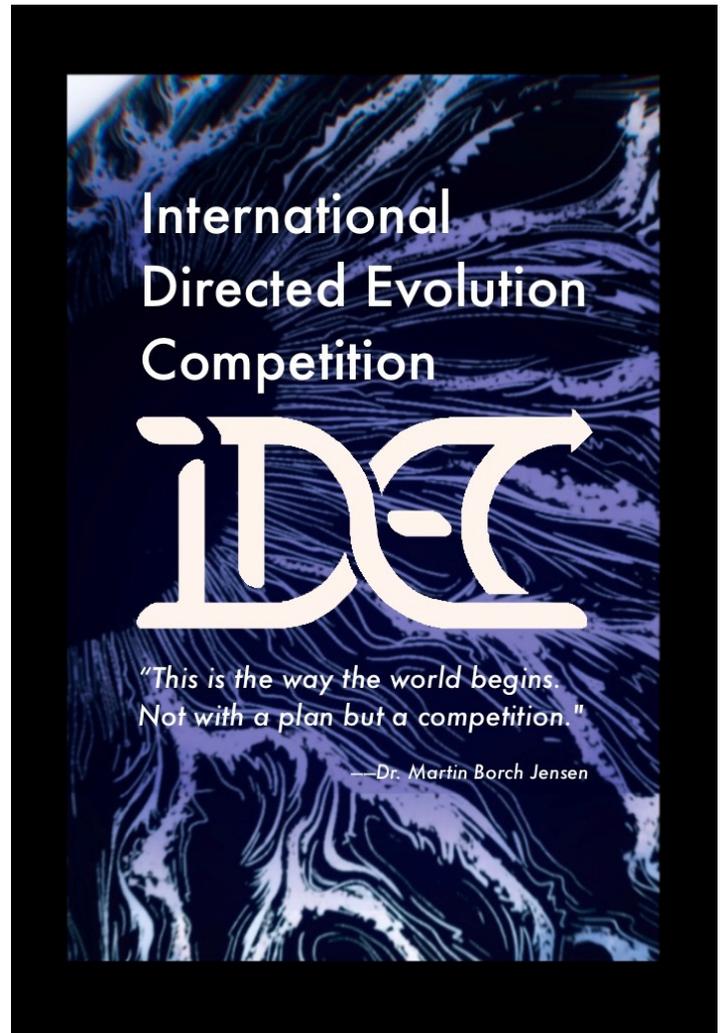
**Friendship Stamp:** We set two bluetooth thermal printers on site.

You can download the APP on your mobile phone, then you can design a stamp pattern or text that represents you, your team, or your project, print it on a sticker, and paste your design, your team's LOGO with your best wish on the handbook of your new friends!



# Contents

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Molecular biology forms the cornerstone of modern directed evolution.

In 2023, we mark the 70th anniversary of a seminal moment in science history: the publication of the DNA double helix structure.

To commemorate this milestone, iDEC 2023 is hosting the iDEC Festival in Cambridge, where the DNA double helix structure was first unveiled.

Following the awards ceremony, there will be a dinner at the Eagle. 70 years ago, Francis Crick famously interrupted patrons' lunch there to declare the discovery of "the secret of life."



## About iDEC

International Directed Evolution Competition (iDEC) is an international initiative focused on creating a scientific community for education, technology sharing, and academic exchange.

Directed evolution, a powerful irrational design approach rooted in rational foundations, will address shortcomings in genetic engineering over the next decade.

Our mission is to inspire young students to harness the creative potential of evolution, arming future bioengineers with the skills to tackle real-world challenges. The synergy of directed evolution technology, youthful creativity, and their innate drive for exploration promises to greatly expand innovation and practical applications, benefiting both the scientific and industrial sectors.

In 2023, the third edition of iDEC is being held on-site for the first time. We warmly welcome students and mentors from around the world to meet and exchange ideas in Cambridge.

## The ethos of iDEC

**innovation**

**Diversity**

**Equality**

**Co-construction & Co-operation.**



## iDEC Founding Story

2019 is the 210th anniversary of Darwin's birth and the 160th anniversary of the publication of the masterpiece *On the Origin of Species*.

A discussion about the future of synthetic biology was sparked by Professor Jamie Davies' article, "Real-World Synthetic Biology: Is It Founded on an Engineering Approach, and Should It Be?"

We concur that synthetic biologists should have the freedom to explore diverse methods, and we recognize the growing significance of directed evolution tools in genetic engineering over the next 5 to 10 years. Thus, the idea of fostering the development and talent cultivation of directed evolution through an international event emerged.

In early 2020, the initial concept of hosting the student competition at either the University of Edinburgh or Cambridge University, both of which were Darwin's alma maters, was proposed. We believe that dedicating the first edition of this competition to the memory of Charles Darwin is both fitting and meaningful.

This idea of iDEC received wide support. 8 students and professors form the board of iDEC as charity trustees. Finally, with the support of young directed evolution enthusiasts, volunteers, and sponsors, iDEC officially started in 2021.

# Schedule

Date	Timelines		Poster
	Time (GMT+1)	Events	
27 <sup>th</sup> Oct.	16:00 – 18:00	Registration (Fitzwilliam college) Collect name badges, conference bags, and hang posters	
	8:00 – 8:40	Registration (Fitzwilliam college) Collect name badges, conference bags, and hang posters	
28 <sup>th</sup> Oct	8:45 – 9:00	Open Ceremony	
	9:00 – 9:25	Opening Speech by Dr. Florian Hollfelder	
	9:30 – 10:00	CPU_CHINA	12
	10:00 – 10:30	OUC-Marine Drugs (online)	06
	<b>10:30 – 11:00</b>	<b>Coffee Break</b>	
	11:00 – 11:30	OUC_DE	10
	11:30 – 12:00	Evolution Suisse	07
	12:00 – 12:30	NNU-China (online)	01
	<b>12:30 – 14:00</b>	<b>Lunch Break</b>	
	14:00 – 14:30	Tongji_China (online)	02
	14:30 – 15:00	USTC-2023 (online)	05
	15:00 – 15:30	NEFU_China	13
	<b>15:30 – 16:00</b>	<b>Coffee Break</b>	
	16:00 – 16:30	Ferroptosis Expedition-NMU_China	09
	16:30 – 17:00	NAU-CHINA-DE	08
<b>17:00 – 18:00</b>	<b>Poster Presentation</b>		
	<b>Time (GMT)</b>	<b>Switch to Winter Time (-1h) at 2:00 AM 29<sup>th</sup> Oct</b>	
29 <sup>th</sup> Oct	9:00 – 9:30	LZU_China	15
	9:30 – 10:00	Tidetron (online)	04
	<b>10:00 – 10:30</b>	<b>Coffee Break</b>	
	10:30 – 11:00	Edinburgh	11
	11:00 – 11:30	WSNJ-A (online)	03
	11:30 – 12:00	NKLMI-NK drug	14
	<b>12:00 – 13:00</b>	<b>Lunch Break and Group Photo</b>	
	<b>13:10– 14:00</b>	<b>Poster Presentation</b>	
	14:30 - 15:30	Lecture by Dr. Thomas Gorochowski Announce Special Awards and Industry Advisory Group award	
	15:30 – 16:00	Lecture by Dr. Ella Watkins-Dulaney	
	16:00 – 17:00	Lecture by Dr. Philipp Holliger	
	<b>17:00 – 17:20</b>	<b>Coffee Break</b>	
	17:20 – 18:00	Announce Single Awards and General Awards	
18:00 – 18:30	Go to the Eagle		
18:30 – 19:30	Dinner		

# Traffic

## Traveling by air:

**Stansted Airport** is the most convenient among London airports, situated just 30 miles away from Cambridge via the M11. **Coaches and trains** are available from Stansted Airport to Cambridge. From **Gatwick and Heathrow airports**, make your way to **King's Cross for a train** to Cambridge. We recommend checking for the most efficient route to Cambridge upon your arrival at the airport.

## Airport to Cambridge by train:

**Stansted Airport:** Inside the Stansted terminal, you will find a railway station where a direct train to Cambridge takes just 35 minutes. Please visit the website to check the train: <https://www.stanstedairport.com/getting-to-and-from/by-train/>

**Heathrow Airport or Gatwick Airport:** There are no direct train connections from Heathrow airport to Cambridge. You can go to central London stations by **Heathrow Express (to London Paddington)** or **Gatwick Express (to London Victoria)** first. For further transfer options, you can visit the website: <https://www.thetrainline.com/> to check the trains.

A frequent train service connects **Cambridge - London**, with trains departing from **Liverpool Street** and **King's Cross stations**. The fastest journey takes just 52 minutes, and during peak hours, there are seven trains per hour.

## Cambridge Railway Station to Fitzwilliam College/Hotel

Cambridge's train station is located to the south of the city center. The town center is roughly midway between the station and Fitzwilliam College. You can easily reach the College/Hotel by taxi or bus.

The 'City Rail Link' bus departs from the station every ten minutes, transporting you to the city center. If you prefer to walk, the journey to the College takes approximately 15 - 20 minutes on foot from the city center.

Please visit <https://www.google.com/> and search the bus information by entering '**Cambridge Station to your destination**'

## Airport to Cambridge by bus

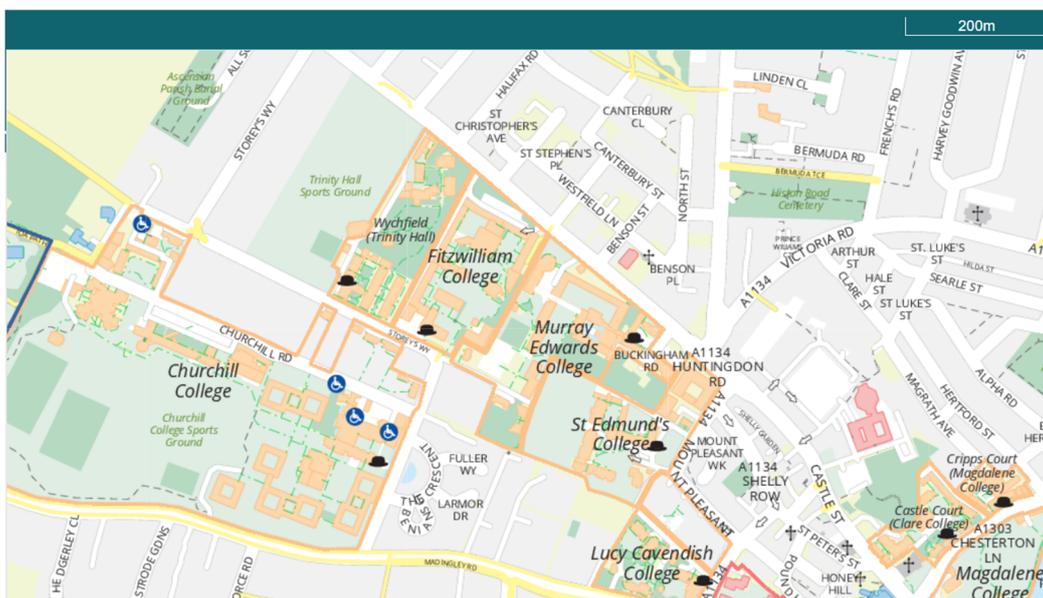
**Stansted Airport:** National Express coaches offer service from London Stansted to Cambridge.

**Heathrow Airport:** National Express coaches offer service from London Heathrow to Cambridge.

Please visit the website: <https://www.nationalexpress.com/en> to find more information.

**Note: Please choose the bus station 'City Centre'.**

**Fitzwilliam College is between Huntingdon Road and Storey's Way, Postcode: CB3 0DG.**



# Online - Gather Town

To facilitate remote participation, Gather Town Space will remain open this year.

We will integrate Zoom with Gather Town to seamlessly blend online and on-site activities. All posters will be displayed synchronously on Gather Town, and our on-site judges will also join online teams for poster presentations through Gather Town.

For teams presenting online, we will collect your poster and presentation slides from **October 22nd to October 23rd**. For teams attending the iDEC Festival in person, we will collect your poster file and presentation slides upon your arrival.

As in previous years, about a week before the iDEC Festival, we will send a test link. We request that all online teams test their network connection, screen sharing, and audio transmission in the Gather Town virtual space prior to the competition. The new step for this year is that online teams will need to install Zoom and test launching the Zoom program within Gather Town.

Based on the situation at the on-site venue, we have decided that all teams will use Gather Town for their presentations directly, and we will also open the Zoom as a backup.

**All online teams need to test your internet speed, Zoom's Function, and try using Gather Town's screen sharing feature.**

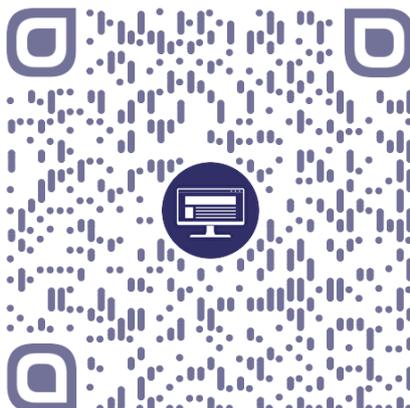
We have allocated some **Breakout Rooms** in Gather Town for online teams, providing them with a separate space for communication and rehearsal before their presentations. The **Breakout Rooms** allocations are as follows:

Date	Timelines		Room
	Time (GMT+1)	Events	
28 <sup>th</sup>	10:00 – 10:30	OUC-Marine Drugs (online)	A in 28 <sup>th</sup>
	12:00 – 12:30	NNU-China (online)	B in 28 <sup>th</sup>
	14:00 – 14:30	Tongji_China (online)	C
	14:30 – 15:00	USTC-2023 (online)	D
	Time (GMT)		
29 <sup>th</sup>	9:30 – 10:00	Tidetrion (online)	A in 29 <sup>th</sup>
	11:00 – 11:30	WSNJ-A (online)	B in 29 <sup>th</sup>

We would like to kindly require that the participants other than the above-mentioned teams should not enter these rooms to avoid disturbing the preparations of other teams.

## Entre Gather Town iDEC 2023: QR code

**Pass Word: 2023**



# CPU\_CHINA

## Rational Design of Norcoclaurine Synthase Using Molecular Simulation and Deep Learning

(9:30 28<sup>th</sup> Oct)

Norcoclaurine synthase (NCS) serves as a biocatalyst that facilitates the condensation of dopamine and 2-Benzenepropanal (2-BPA) into Tetrahydroisoquinoline (THIQs) derivatives, exhibiting significant potential as prodrugs. However, the current body of knowledge indicates that most THIQs derivatives are synthesized chemically, resulting in various drawbacks. NCS presents a promising biological alternative for THIQs synthesis. Regrettably, the absence of in-depth understanding regarding the catalytic mechanism has resulted in inefficient allocation of resources during pure evolutionary approaches. This limitation impedes the optimization of NCS's industrial production. To surmount these challenges, we employed molecular dynamics (MD), quantum chemical calculations and other rational tools to reveal catalytic mechanism, which may benefit the redesign of NCS in the future. At the same time, heterocyclic tetrahydroisoquinoline derivatives are another promising class of drug precursors. We have made efforts to expand NCS's adaptability to heterocyclic substrates and have achieved some results. Additionally, we have developed a  $K_{cat}$  prediction deep learning machine that shows potential in predicting enzyme  $K_{cat}$  values.

## OUC-Marine Drugs

### Semi-rational directed evolution of P450BM3 for enhanced activities in acidic/alkaline conditions

(10:00 28<sup>th</sup> Oct)

The alkaline- or acid-stable enzymes are more advantageous for agricultural and industrial applications. Cytochrome P450BM3 is a biotechnologically important and versatile enzyme capable of producing various drug metabolites. However, the engineering of physicochemical properties of P450BM3 remains scarce. In this project, we first selected 4-nitrophenyl acetate and 4-nitrophenyl butyrate as the substrates of P450BM3. We then applied semi-rational directed evolution strategy to engineer P450BM3 for enhanced activities in acidic/alkaline conditions. We analyzed the possible residues on the surface that may be closely related to the optimum pH of P450BM3, and constructed a virtual of 380 saturated mutants. By using DynaMut website calculation, the top7 mutants with enhanced stabilities were selected and expressed in *E. coli*. The K24I and D422W variants were screened out to exhibit ~0.5-fold and 0.4-fold increased activities toward 4-nitrophenyl acetate in acidic condition (pH=6.0). Our study provides foundation for further engineering of P450BM3 to adapt acidic/alkaline conditions for practical use.





## OUC\_DE

### Directed Evolution of Tunable Bistable Switch for Cellular Metabolic Regulation

(11:00 28<sup>th</sup> Oct)

Bistable switches are ubiquitous in natural and engineered biological systems, playing a key role in cellular regulation. We constructed a bistable switch consisting of tetracycline operon, arabinose operon, and lactose operon, allowing for the artificial control of the rate at which cells absorb metabolites from their environment and direct the flow of carbon within the cell. This aims to achieve rapid growth of engineered bacteria and efficient production of target metabolic products. We employed error-prone PCR and machine learning-assisted directed evolution to optimize the bistable system, increasing its tunability. Mutants were analyzed by observing fluorescence intensity and using visualization tools such as Pymol and molecular docking, to identify those that bind tightly to DNA and loosely to inhibitors. Eventually, we individually screened out an *araC* and *tetR* mutant that theoretically bind tighter with DNA and show better inhibition effect compared with the wild type.

## Evolution Suisse

### Evolving a Plant Pattern Recognition Receptor to Gain Resistance to a Pathogen-Derived Effector by Using a Novel Reverse Yeast Two-Hybrid System

(11:30 28<sup>th</sup> Oct)

As the first layer of plant immunity, plants use pattern recognition receptors (PRRs) to perceive the existence of pathogens. To counteract PRRs, pathogens secrete effectors that inhibit PRR's functions. In this study, we aim to develop a new strategy to enhance crops' disease resistance by engineering PRRs to elude the attack of effectors, using a directed evolution approach. As a proof of concept, we worked on disrupting the interaction between pathogen effector AvrPtoB and plant immune receptor CERK1. To achieve this, we developed a novel reverse yeast two-hybrid (rY2H) system, TRUST-rY2H (Truncation Resistant and Universal Self-cleaving peptide Technology reverse yeast two-hybrid), which is resistant to a high rate of truncation mutations and can be universally applied to different genetic protein-protein interaction assays. Combining this novel rY2H system with a computational prediction method, we successfully identified mutations disrupting AvrPtoB-CERK1 interaction. An in-planta screening system was also developed to identify bona fide AvrPtoB-resistant CERK1. This method not only has potential applications in PPI disruption and pathogen resistance but also opens avenues for future explorations in other realms.

# NNU-China

## Corner Engineering: A Directed Evolution Strategy for Enhancing Enzyme Resistance in Deep Eutectic Solvents (12:00 28<sup>th</sup> Oct)

As a green and cost-effective solvent, deep eutectic solvent (DES) shows promise in biocatalysis. However, enzyme activity in DESs is often inhibited, limiting their application. To address this, our project proposed a directed evolution strategy called Corner Engineering. Using *Bacillus subtilis* lipase A (BSLA) as a model, we thoroughly validated the effectiveness of the strategy and optimized it. Notably, the variant M137D/N138D displayed an impressive 3.0-fold increase in resistance compared to the WT in 95% (v/v) ChCl:ethylene glycol. To confirm the versatility and effectiveness of our optimized approach, we conducted validation experiments on *Bacillus subtilis* esterase (Bs2Est). In the 75% (v/v) ChCl:ethylene glycol, the resistance of these variants could reach up to 3.1-fold, thus affirming the broad applicability of our engineered enzyme strategy. The molecular investigations reveal that increased water molecules at substrate binding sites are the dominant determinant of elevated resistance, indicating a promising avenue for understanding enzyme-DES interactions.



## Time for Lunch

### Vegetarian:

**Feta Cheese Filled Pepper (Gluten Friendly)**

### Warm:

**Sticky Chicken Wings (Gluten Friendly)**

**Beef Chilli Meat Balls**

**Panko Breaded Prawns**

### Dessert:

**Choux Buns with Chocolate Sauce**



## Tongji\_China

### Semi-rational Directed Evolution of Electrically Conductive Pili Based on Adaptive Particle Swarm Optimization Design

(14:00 28<sup>th</sup> Oct)

The type IV pili of *Geobacter metallireducens* exhibit an exceptional electrical conductivity of up to 277 S/cm at pH 7, making them the most conductive biological nanomaterials known to date. The overlapping  $\pi$ - $\pi$  orbitals of aromatic moieties imparts metallic conductivity to these revolutionary "green" nanomaterials. We build an antibody detection system, and the conductivity of this pili is the key to maintaining stability and accuracy of our system. We use optimization methods of mathematical modeling combined with protein directed evolution to attempt to optimize the structure of this pili to improve its conductivity. We find 5 possible mutation sites (V9, A20, S34, D54, T56) may improve the maximum conductivity of e-pili. Combing with an innovative screening method based on the microbial fuel cell system, we may eventually obtain a pili with higher conductivity.

## USTC-2023

### Continuous Directed Evolution and High-throughput Screening for Difficult-to-detect Substances

(14:30 28<sup>th</sup> Oct)

Directed evolution is a powerful synthetic biology approach used to optimize proteins especially for enzyme. It is commonly employed to enhance the catalytic efficiency of target enzymes to meet production demands. EvolvR systems including enCas9 and error-prone DNA polymerase have been developed to enable continuous directed evolution in *Escherichia coli* and *Saccharomyces cerevisiae*, yielding promising results. However, sensitive and high-throughput substrate/product detection technologies are urgently needed for the directed evolution of certain synthetic enzymes. Many substances, such as cyclic monoterpenes and monosaccharides, are difficult to detect endogenously in real-time. Here, we aim to expand the application of EvolvR to nonconventional yeast species and establish synthetic platforms for two difficult-to-detect compounds, borneol and tagatose. Additionally, we have developed biosensors capable of endogenous detection, in order to facilitate directed evolution pathways for difficult-to-detect substances and provide a paradigm for similar molecules.

## NEFU\_China

### Directed evolution of key enzymes in the synthesis of 4-hydroxymandelate pathway

(15:00 28<sup>th</sup> Oct)

In this study, we employed metabolic engineering and directed evolution strategies to investigate and address two key challenges, including insufficient precursor supply and limited activity of crucial enzymes, in the biosynthesis of 4-hydroxymandelate (HMA), a high-value aromatic compound. Through gene overexpression and multi-level gene interference using the CRISPRi approach, we successfully engineered an *E. coli* chassis strain capable of stably producing the essential substrate 4-hydroxyphenylpyruvate (HPP) and the titer reached 0.91 g/L. In a high-throughput screening process using a biosensor based on allosteric transcription factors, we eliminated the reliance on expensive equipment. The activity of the key enzyme and the viability of the strain were coupled through directed evolution. We eventually obtained a mutant clone, HmaSV152G, with a 125% improvement in the catalytic rate. In its fermentation, we achieved the high production of 3.63 g/L HMA in 24 h with a single supply of 20 g/L glucose.

## Ferropoptosis Expedition-NMU\_China

### Directed Evolution of Sorafenib Resistant Strains to Identify Genes and Molecular Mechanisms Driving Resistance

(16:00 28<sup>th</sup> Oct)

In recent years, liver cancer has become the third leading cause of cancer-related deaths, and the vast majority of liver cancers are hepatocellular carcinoma. Sorafenib is the first-line systemic therapy for the advanced hepatocellular carcinoma. However, numerous patients respond poorly to sorafenib or develop resistance after months of treatment. Therefore, there is an urgent need to explore the underlying mechanism of sorafenib resistance. By constructing HepG2 sorafenib resistant cell line and performing RNA sequencing, our study identified that KDELR3 could promote HCC sorafenib resistance by inhibiting ferroptosis. Therefore, targeting KDELR3 may offer a potential combination strategy to reduce sorafenib resistance in HCC.





## NAU-CHINA-DE

### Directed evolution of the FdeR allosteric transcription factor and a riboswitch to construct a liquiritigenin biosensor toolkit

(16:30 28<sup>th</sup> Oct)

Liquiritigenin, a dihydroflavonoid produced by secondary plant metabolism, has broad applications in food and pharmaceutical industries. However, the production of liquiritigenin still relies on low-yield plant extraction and chemical synthesis currently. Here, we developed biosensors that could identify liquiritigenin specifically based on allosteric transcription factors and riboswitches, enabling the evolution of biomolecules with highly specific new activities. In our future work, we aspire to demonstrate the potential of directed evolution in optimizing biosensors. We are committed to applying the evolved biosensors to intracellular detection of liquiritigenin synthesis and screening of liquiritigenin high yielding strains, thus providing a solution for high yielding biosynthesis of liquiritigenin.

## Poster Presentations (17:00 - 18:00 GMT+1, 28<sup>th</sup>, 13:10 – 14:00 GMT, 29<sup>th</sup>)

TEAMS	NO.	LOCATION
NNU-CHINA	1	Online
TONGJI_CHINA	2	Online
WSNJ-A	3	Online
TIDETRON	4	Online
USTC-2023	5	Online
OUC-MARINE DRUGS	6	Online
EVOLUTION SUISSE	7	On-site
NAU-CHINA-DE	8	On-site
FERROPTOSIS EXPEDITION-NMU_CHINA	9	On-site
OUC_DE	10	On-site
EDINBURGH	11	On-site
CPU_CHINA	12	On-site
NEFU_CHINA	13	On-site
NKLMN-NK DRUG	14	On-site
LZU_CHINA	15	On-site

# LZU\_China

## Exploring a transformative model for preventing hypercholesterolaemia: directed evolution of *E. coli* Nissle 1917 to obtain gene combinations with superior cholesterol-regulating effects

(9:00 29<sup>th</sup> Oct)

Hypercholesterolemia is one of the major influencing factors of cardiovascular disease (CVD). Traditional lipid-lowering drugs such as ezetimibe have unavoidable drug side effects. The method of preventing hypercholesterolemia by reducing cholesterol absorption through intestinal microbiota, and then preventing CVD, may become a transformative model. Based on this, the LZU-China iDEC team is trying to use the IsmA gene that can directly metabolize cholesterol, the BCoAT gene that affects cholesterol absorption, and the BSH gene that promotes bile acid excretion to construct engineering *E. coli* Nissle 1917(ECN). We selected and optimised our effector gene modules by means of directed evolution to obtain combinations of genes with better cholesterol-regulating effects, and attempted to screen the optimal set of strain designs by means of directed evolution. We validated the function of the oleic acid inducer under both aerobic and anaerobic conditions, and proposed a design for directed evolution of the oleic acid inducer.

## Tidetrone

### Strengthen the biosynthesis of human collagen III by multi-dimensional engineering strategies

(9:30 29<sup>th</sup> Oct)

Collagens have strong preferences for amino acids, modifications, and repeated structures, making them difficult to biosynthesize. Here, we developed multi-dimensional engineering strategies to improve collagen synthesis. In transcription layer, we optimized the Phage-Assisted Non-Continuous Evolution method and obtained the T7 RNA polymerase mutant (K345E and P474L) that possessed 2.3-fold higher performance in CO3A1 gene transcription. In post-translational modification layer, we screened 19 monosubunit prolyl 4-hydroxylases (P4H) using structure-based protein clustering, and developed a Fluorescence-Activated Droplet Sorting method coupled target enzymatic mutagenesis to filter the moumouvirus P4Hc mutant ( $\Delta$ 2-23, S109P, L122F, V169I and P181Y) with 2.6-fold stronger activity to hydroxylate CO3A1 protein. Moreover, in RNA stability and translation layer, we improved the cell-free protein synthesis system using metabolic compensation and autocyclization ribozyme in vitro, which greatly increased the yields of CO3A1 and ELN to 0.31 and 2.58 g/L, respectively. These findings are important for the industrial production of collagens.





## Edinburgh

### Exploring the Possibilities and Challenges of enhancing Salinity tolerance in *Synechocystis* sp. PCC 6803 by directed evolution

(10:30 29<sup>th</sup> Oct)

Cyanobacteria are incredibly versatile microorganisms which have numerous applications in biotechnology. However, mining cyanobacteria for diversity and using them as a chassis has proven difficult due to the limited number of fully annotated genomes available. In the present study, we aim to generate a strain of *Synechocystis* sp. PCC 6803 with increased salt tolerance through directed evolution. Glucosylglycerol phosphate synthase is the key enzyme in the pathway for glucosyl glycerol, an osmolyte which confers salt tolerance in *Synechocystis* sp. PCC 6803. This pathway can be reconstituted in *Escherichia coli* allowing a rapid acceleration in the timespan necessary to perform directed evolution. The native *Synechocystis* gene *ggps* was extracted from the genome and error prone PCR was performed to generate a mutant library and this library was assembled into a level 1 construct. An assay was designed utilising the Edinburgh Genome Foundry automated robotic laboratory allowing for large high throughput selection.

## WSNJ-A

### Engineering of *Clostridium tyrobutyricum* to create engineered strains more suitable for directed evolution

(11:00 29<sup>th</sup> Oct)

Directed evolution of promising engineered strains to improve their production capacity has received widespread attention in recent years. This study aims to develop a robust *C. tyrobutyricum* chassis which has an alternative non-oxidative glycolysis (NOG) pathway to EMP pathway and can withstand possible growth side effects of EMP modification during genomic directed evolution for enhanced or expanded synthesis capacity of bioproducts. We integrated a non-oxidative glycolysis (NOG) pathway to EMP pathway in *C. tyrobutyricum* by introducing F/Xpk gene. Plasmids using two F/Xpk genes and three different native promoters,  $P_{thl}$ ,  $P_{tkl}$  and  $P_{fba}$ , were constructed and transferred into *C. tyrobutyricum* L319. By analyzing the growth and yields of butyric acid and acetic acid of the strain, we found that F/Xpk gene derived from *C. acetobutylicum* and  $P_{tkl}$  promoter was the best combination for constructing NOG pathway in *C. tyrobutyricum*, and xylose was the best carbon source for the strain.

# NKLM1-NK drug

## A genome-scale gain-of-function CRISPR screen in NK cells identifies energy metabolism as a means to enhance CAR-NK therapy

(11:30 29<sup>th</sup> Oct)

The utilization of chimeric antigen receptor (CAR)-natural killer (NK) cells therapy has shown promise as an immunotherapeutic strategy in combating hematological malignancies. Nevertheless, this therapy encounters various challenges, notably the tumor microenvironment (TME). The identification of an appropriate methodology and molecular target for modifying NK cells to achieve desired functionality under the immunosuppressive pressure of the TME holds significant implications for NK cell-centered therapies. In this study, we employed a CRISPR activation screen library utilizing dead-guide RNA (dgRNA) in NK cells and identified MTCH2, a gain-of-function (GOF) target, notably augmented the functionality and longevity of NK cells in pancreatic cancer. Furthermore, the overexpression of MTCH2 in CAR-NK cells exhibited heightened cytotoxicity in eradicating tumors in vitro and in vivo. Moreover, MTCH2-overexpression augmented ATP production, thereby promoting cytotoxicity within the TME. These results collectively establish a screening method for identifying GOF agents for enhancing the efficacy of CAR-NK therapy.



## Time for Lunch

### Vegetarian:

**Stuffed Courgette with Ricotta Cheese (Gluten Friendly)**

### Warm:

**Sticky Chicken Wings (Gluten Friendly)**

**Duck Spring Roll**

**Tempura Battered Goujons**

### Dessert:

**Chocolate Brownie**

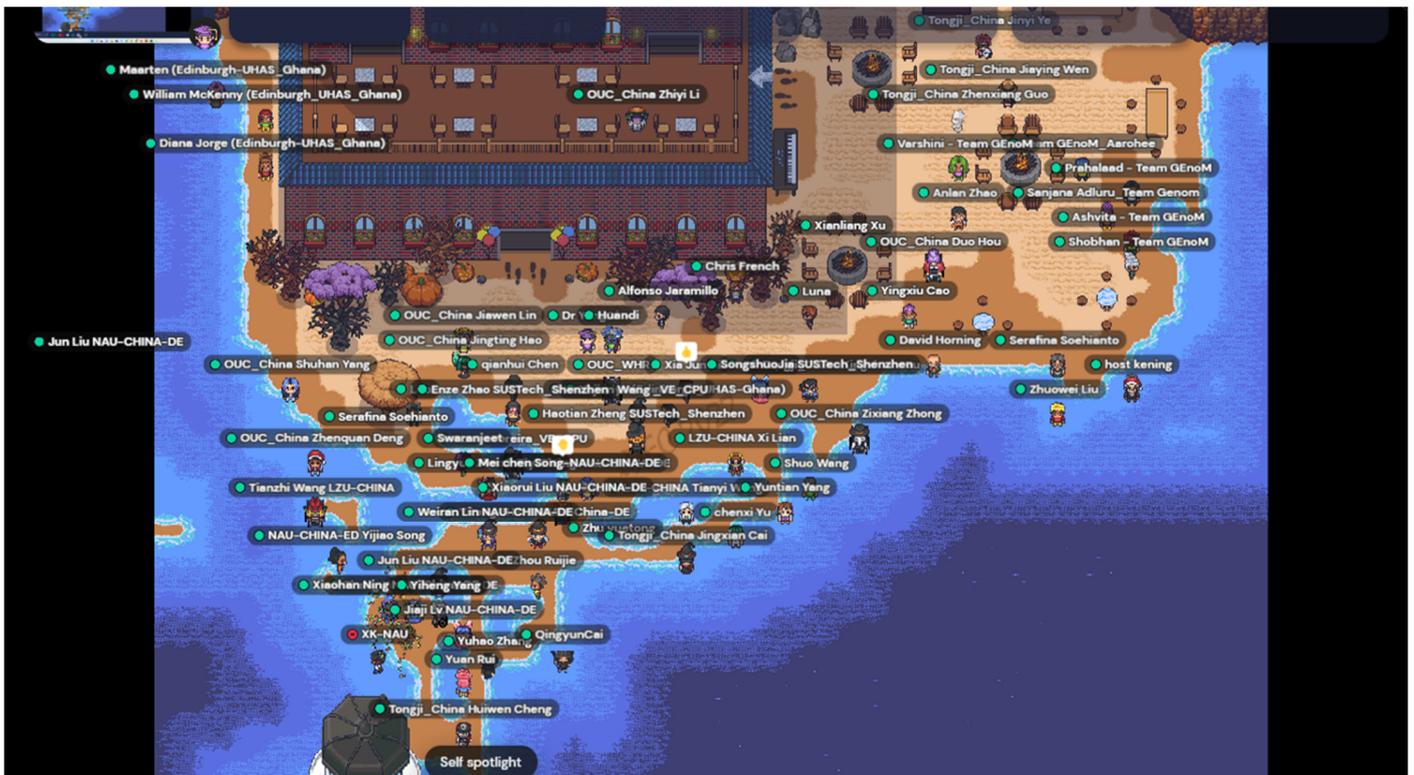
# Group Photo

Group photos are divided into online and on-site.

**The online photo session time is 13:00 GMT 29th Oct.**

The location for the online group photo is on the beach outside the Gather Town venue. Please choose your favorite look for your avatar, and choose a location on the beach where everyone can see you.

**The online group photo will be made into a postcard and sent to each contestant as a souvenir.**



**The on-site photo session time is 12:45 GMT 29th Oct.**

The location for the on-site group photo is in front of the Grove.

Our volunteers will guide everyone to the photo location after lunch. Offline photos will also be made into postcards as souvenirs.



- Presentations and Posters: Auditorium
- Lunch: Cafe Bar (12)

# Invited Speakers

iDEC HQ is honored to invite three senior scientists in the field of directed evolution to bring invited lectures to our participants.

The topics of the three invited lectures jointly outline the core themes that contributed to the creation of iDEC:

## iDEC Festival 2023



### Awards Ceremony Lectures

Registration QR code  
29th Oct 14:30-17:00 GMT



#### Engineering is Evolution: Perspectives on the Role of Evolution in Biological Design

**Dr. Thomas E. Gorochowski**

Associate Professor of Biological Engineering  
Co-Director, Bristol BioDesign Institute (BBI)  
School of Biological Sciences, University of Bristol



#### The Nature of Directed Evolution: Past, Present, and Future

**Dr. Ella Watkins-Dulaney**

Lead Protein Engineer at Aralez Bio



#### Synthetic Genetics: Beyond DNA and RNA

**Dr. Philipp Holliger**

Program Leader at MRC Laboratory of Molecular Biology (MRC-LMB)  
Member of European Molecular Biology Organization (EMBO)

# Acknowledgment

iDEC 2023 could not be successfully organized without the help of our sponsors, collaborators, iDEC HQ members and participants.

We thank **Bluepha** and **New England Biolabs** for their generous support.

## **iDEC 2023 Invited Speakers:**

Dr. Florian Hollfelder from Cambridge University

Dr. Thomas Gorochowski from the University of Bristol

Dr. Philipp Holliger from the MRC Laboratory of Molecular Biology (LMB)

Dr. Ella Watkins-Dulaney from Aralez Bio

Dr. Benjamin Porebski from the MRC Laboratory of Molecular Biology (LMB)

Dr. Rongzhen Tian from the MRC Laboratory of Molecular Biology (LMB)

## **iDEC 2023 Judge List:**

Dr. Ana González-Rueda from the MRC Laboratory of Molecular Biology (LMB), UK

Dr. Bryce Clifton from the MRC Laboratory of Molecular Biology (LMB), UK

Dr. Chang Liu from UC Irvine, US

Dr. David Horning from the Salk Institute, US

Dr. Ella Watkins-Dulaney from Aralez Bio, US

Dr. Fabian Rehm from the MRC Laboratory of Molecular Biology (LMB), UK

Dr. Fankang Meng from the Imperial College London, UK

Dr. Jamie Davies from the University of Edinburgh, UK

Dr. Jin Yin from Bluepha, CN

Dr. Kenneth Wu from the MRC Laboratory of Molecular Biology (LMB), UK

Dr. Rongzhen Tian from the MRC Laboratory of Molecular Biology (LMB), UK

Dr. Xiao Yi from the SIAT, CN

Dr. Yangqi Gu from the MRC Laboratory of Molecular Biology (LMB), UK

## **iDEC Executive Committee Members:**

Prof. Jamie Davies, Prof. Tom Ellis, Prof. Chris French, Shan Jiang, Dr. Nadanai Laohakunakorn, Dr. Yang Liu, Dr. Zakir Tnimov, Prof. Ye Chen, Prof. Chang Liu.

## **iDEC 2023 Organizers:**

Dr. Trevor Y. H. Ho, Chong Teng, Yinan Ren, Katherine Martin, Jiayi Zeng, Kening Chen, Tong Lyu, Huandi Xu, Stefan Bassler, Dr. Svenja Vinke, Gokul Bhaskaran, Levin Joe Klages, Irina Rais, Swaranjeet Singh, Dr. Yang Liu, Kenneth Wu, Dr. Meng Su, Dr. Fabian Rehm, Dr. Ganesh Agam, Dr. Nikos Nikolopoulos, Talal Haddad, Dr. Bryce Clifton, Dr. Sara Clifton, Dr. Yangqi Gu, Dennis Wang.

## **iDEC 2023 Sponsor Representatives:**

Geng Qiang from Bluepha and Erin Varney from New England Biolabs.

## **iDEC 2023 Teams:**

NNU-China, Evolution Suisse, Tongji\_China, NAU-CHINA-DE, Ferroptosis Expedition-NMU\_China, OUC\_DE, WSNJ-A, Tidetron, Edinburgh, USTC-2023, CPU\_CHINA, OUC-Marine Drugs, NEFU\_China, NKLM-I-NK drug, LZU\_China, PicoPals.

## Sponsors & Collaborators

iDEC is generously supported by our sponsors and collaborators to carry out public welfare education and young talents in scientific and technological innovation.

This year, our golden sponsor Bluepha provided iDEC with strong financial and industry-related support again.



The iDEC Special Awards are titled by our Gold Sponsor Bluepha as:

### **Bluepha Reporter System Award**

Award to teams who develop or optimize a reporter system and use it in their iDEC projects.

### **Bluepha Library Constructing Award**

Award to teams that optimize or establish novel methods for genetic diversification in their research.

### **Bluepha Screening Assay Award**

Award to teams who establish or optimize screening assays in their projects.



At the same time, iDEC 2023 has received strong support from more iDEC sponsors.

We are grateful for the generous support from the industry:



For more information about iDEC sponsors, please read our sponsor pages.

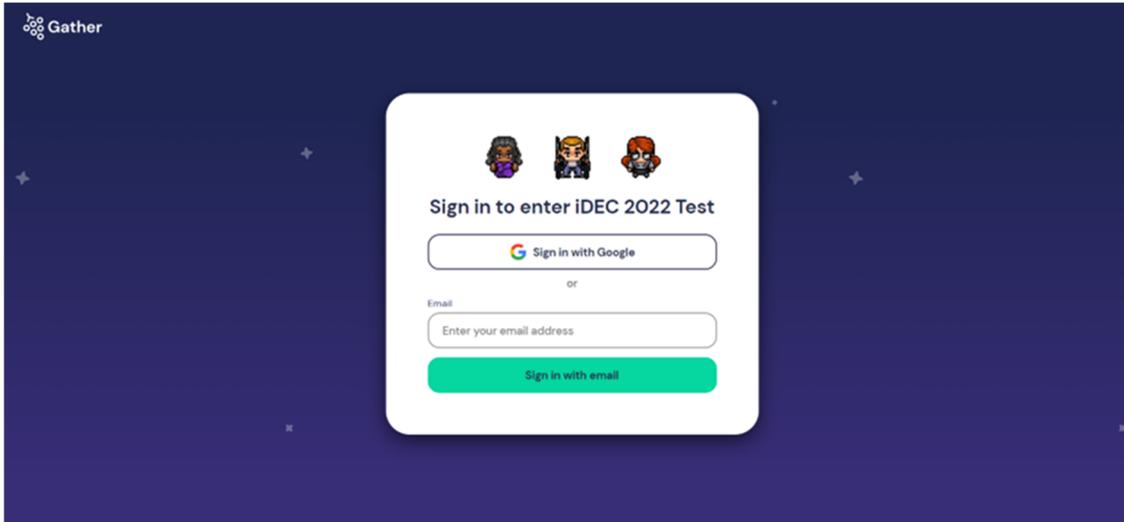
We also maintain collaboration with the non-profit organization Regenesys, the Møller Institute (Cambridge University), and the Fitz Events.



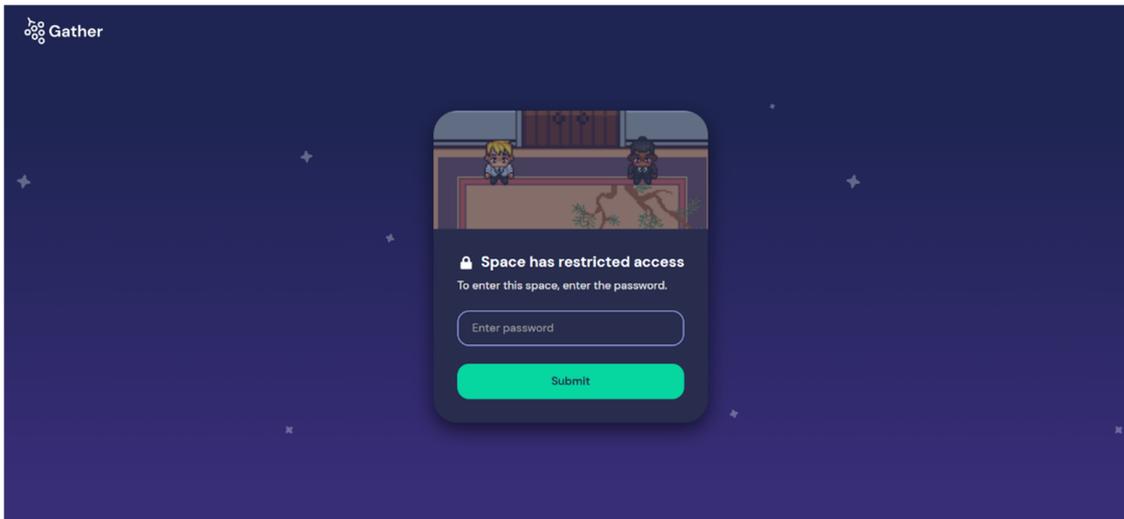
# Gather Town Guide

2D virtual platform Gather Town is used for the online iDEC Festival.

All team members will receive a link to join Gather Town before the opening ceremony. Here is a simple guide on how to use Gather Town.



Every participant must sign in before entering the iDEC 2023 space by the link we send. **The password will be '2023'**.



In the Gather virtual environment, you can set your own image and move freely. When the virtual character is close to others, you can hear each other's voices.

You can also find tables and chairs placed on the carpet in the virtual venue. The carpet area is a private space where only virtual characters who enter the carpet region can talk.

iDEC HQ have built breakout rooms for the iDEC teams. The iDEC team can prepare presentations without interruption in a separate virtual room.

In the poster display area, we will hang the posters of each team and marked them with number. During the poster presentation, the judges will visit the poster from time to time and listen to the introduction of the poster content by the team.

The carpet area in front of the poster is a soundproof space, and only people who enter the area can talk to each other.

iDEC 2023  
Gold Sponsor



**Bluepha** is a biomanufacturing and material innovation company providing breakthrough products based on synthetic biotechnology. Founded in October 2016, Bluepha has been actively committed to the design, development, manufacture, and marketing of new bio-based molecules and materials, including:

- Bio-polymers PHAs which are biodegradable in any environment without leaving harmful footprints
- Materials for regenerative medicine
- Novel functional ingredients for personal care and medical beauty
- New food additives
- Probiotic products, etc.

The glory of Bluepha is inseparable from the core team coming from top research institutes such as Tsinghua University, Peking University, Chinese Academy of Sciences and the Fortune Global 500. A dream team of experts and consultants is composed of leaders in the field of SynBio industry, education, and research.

In 2022, the first product pipeline of Bluepha with a super-factory of marine degradable material PHA: Bluepha™ was officially started construction in Binhai, Yancheng, Jiangsu, with annual production capacity of 25,000 tons. The performance of Bluepha™ has been verified by several enterprise customers from Fortune Global 500, and has obtained orders and intentional orders from many enterprises. At present, Bluepha has signed strategic cooperation agreements with a few partners worldwide to expand the global market with unlimited potential of Bluepha™.

In addition, Bluepha has reserved dozens of R&D pipelines for new products. The application scenarios cover the fields of health & medical care, agricultural environmental protection, beauty & cosmetic and innovative food. Each product pipeline corresponds to a direct market size of more than \$1 billion.

Since establishment, the Bluepha has built an interdisciplinary team composed of senior scientists and engineers in different fields such as robotics, software development, mechatronics, big data, and synthetic biology. An automated and datamated infrastructure "Synbio OS" was set up. It is expected that in the next 3 years, the R&D cycle of a single Bluepha product pipeline will be shortened by 70% on the existing basis.



*be* INSPIRED  
*drive* DISCOVERY  
*stay* GENUINE

# Putting science first.

## Post-Doctoral Fellowships at New England Biolabs®

Established in the mid 1970s, New England Biolabs, Inc. (NEB®) is the industry leader in the discovery and production of enzymes for molecular biology applications and now offers the largest selection of recombinant and native enzymes for genomic research. NEB continues to expand its research and development into areas related to DNA replication, programmable nucleases, epigenetics, molecular parasitology, sample preparation for next generation sequencing, synthetic biology, glycobiology and RNA analysis.

Scientists in the Research Department at New England Biolabs conduct basic research in the areas of Molecular Enzymology, Nucleic Acid Replication, Protein Expression and Modification, Genome Biology and RNA Biology. The Post-Doctoral Fellowship program at NEB aims to train recent Ph.D. graduates in a modern industrial molecular biology setting. Post-doctoral fellows conduct basic research, publish in high quality journals and present at scientific conferences.

Employment at NEB offers a stimulating and creative work environment in a state-of-the-art research and production facility, with a team of exceptional scientists and professional staff. The NEB culture emphasizes personal and professional growth through creativity, teamwork, respect and responsibility, while maintaining a casual campus-like working environment. Our diverse and talented team of scientists enjoy a collaborative research environment with much of the freedom and intellectual challenge of academia. Our unique corporate philosophy encourages dialogue and innovation.

For information about Post-Doctoral Fellowships at New England Biolabs please visit: <https://www.neb.com/about-neb/careers>



deoxyribose nucleate from calf thymus. Structure B

each unit being shielded by a sheath... each unit is then free to take up its... configuration independently of its neighbor... it is highly likely that the general form... If we adopt the hypothesis of a helix... it is immediately possible to make... of structure B, to make... of nature and dimensions... innermost maxima... layer lines lie... radiating from the origin... helix the structure... on by:

$$F_n = J_n(2\pi rR) \exp$$

$J_n(u)$  is the  $n$ th-order Bessel function of  $u$ ,  $r$  is the radius of the helix, and  $R$  and  $\psi$  are the radial and azimuthal co-ordinates in reciprocal space; this expression leads to an approximately linear array of intensity maxima of the type observed, corresponding to the first maxima in the functions  $J_1, J_2, J_3$ , etc. If, instead of a smooth helix, we consider a series of residues equally spaced along the helix, the transform in the general case treated by Crick, Cochran and Vand is more complicated. But if there is a whole number,  $m$ , of residues per turn, the form of the transform is as for a smooth helix with the addition, only, of the same pattern repeated with its heights  $mc^*$ ,  $2mc^*$  ... etc. ( $c$  is the fibre-

# MOLECULAR STRUCTURE OF NUCLEIC ACIDS

## Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the deoxyribose nucleic acid (D.N.A.) which has novel features which are of considerable interest.

The structure for nucleic acid has already been described by Pauling and Corey<sup>1</sup>. They kindly made their model to us in advance of publication. It consists of three interlocking phosphate groups near the fibre axis. The phosphates are on the outside of the helix. In our opinion, the material for two reasons: (1) it is not clear what forces hold the phosphate groups together, especially as the phosphate groups near the axis will be small. (2) the van der Waals forces between the phosphate groups has also been suggested.

In his model the phosphate groups are bonded to the bases on the inside of the helix. This is not defined, and for the following reasons: (1) It has not been suggested for deoxyribose nucleic acid. (2) It is possible with a ribose nucleic acid the extra oxygen atom under Waals contact. The previous model of our structure is compatible with the following experimental details of the structure on published arguments.



...-axis period is 34 A. ... lies on the ...



# International Directed Evolution Competition 2023

This is the way the life begins  
Not with a plan but a competition

