Guru Nanak Centre for Research

Event Title	**NATIONAL WEBINAR ON "THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP"**	
Category	UG/PG STUDENTS, RESEARCH SCHOLARS AND FACULTY, PROFESSIONALS AND INDUSTRY PERSONS	
Date	**From : 1.10.2020**	**To : 1.10.2020**
No. of Resource Person	**1**	
No. of Participants	1000	

1. Report Description:

The Guru Nanak Centre for Research (GNCR) of the Guru Nanak College (Autonomous), Velachery, Chennai organised the **NATIONAL WEBINAR ON "THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP"** on 1st October 2020 from 12.00 Noon to 1.30 p.m. with the aspiration to highlight the significance of the role of transgenic fishes in Drug Development and the enormous scope and opportunities available for entrepreneurship. This National Webinar was planned and well accomplished by Dr. J. Jayanthi, Dean Research, Guru Nanak Centre for Research (GNCR) under the able direction of our Most Revered General Secretary & Correspondent, Sardar Manjit Singh Nayar and constant support from our Respected Principal, Dr. M. G. Ragunathan.

The **NATIONAL WEBINAR ON "THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP"** was inaugurated by our Respected Vice Principal (Student's Affairs) Dr. L.R.S. Kalanithi with the Welcome Address. Vice Principal Madam welcomed the Resource Person, Dignitaries of the College Management, Faculty from Guru Nanak College and the participants from across the Globe who joined virtually. The Theme of the Webinar was introduced by the Convener of the webinar, Dr. J. Jayanthi, Dean Research of Guru Nanak Centre for Research. Dr. J. Jayanthi, Dean Research mentioned that huge responses were received from more than 800 registrations and the webinar

programme was livestreamed in YouTube on our official channel “GURU NANAK CENTRE FOR RESEARCH”.

Dr. Mahendrakumar. M, Assistant Professor, Department of Biotechnology, Guru Nanak College (Autonomous), Chennai introduced the Resource Person, **Prof. S. G. PRAKASH VINCENT,** Professor & Head, Centre for Marine Science and Technology, Rajakamangalam Campus, Kanniyakumari, Manonmaniam Sundaranar University, Tamil Nadu. Dr. S. G. Prakash who is a DAAD Fellow (Germany) during his Ph.D. Dr. Prakash who is holding many positions in academic and research portfolios which includes EMBO WP Fellow (Germany), UNESCO Fellowship Awardee (Italy), Mariecurie Fellow (EMBL), Chairman Associate – BRICS Biomed Consortium and he is the FOCAL POINT, European Commission HORIZON 2020.

Dr. S.G. Prakash very clearly explained the step by step process involved in Drug Discovery and explained the various benefits and advantages of using transgenic fishes at various level of Drug Development and testing the efficiency of a lead drug molecule. He also narrated the different diseases for which drug development have been possible using transgenic fishes. Dr. S. G. Prakash also gave a vivid picture about the huge entrepreneurial opportunities available for Start Ups regarding Drug Discovery and Development. The resource person Dr. S.G. Prakash answered all the questions raised and clarified all the doubts of the participants.

Dr. J. Jayanthi, Dean Research narrated the important points of the presentation of Dr. S.G. Prakash in her concluding Report of the **NATIONAL WEBINAR ON “THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP”**. The Webinar ended well with the Vote of Thanks delivered by the Organising Secretary of the Webinar, Dr. Mahendrakumar. M, Assistant Professor, Department of Biotechnology, Guru Nanak College. All the Participants were given a certificate of participation.

2. Invitation

GURU NANAK COLLEGE (Autonomous)

Re-accredited at 'A' Grade by NAAC
Affiliated to the University of Madras
Guru Nanak Salai, Velachery, Chennai – 600 042.

GURU NANAK CENTRE FOR RESEARCH (GNCR)

NATIONAL WEBINAR ON

"THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP"

DATE : 1st OCTOBER 2020 | TIME : 12.00 Noon – 1.00p.m.

RESOURCE PERSON **Prof. S. G. PRAKASH VINCENT**

Professor & Head,
Centre for Marine Science and Technology,
Manonmaniam Sundaranar University, TN

DAAD Fellow (Germany)
EMBO WP Fellow (Germany)
UNESCO Fellowship Awardee (Italy)
Mariecurie Fellow (EMBL)
Chairman Associate – BRICS Biomed Consortium
FOCAL POINT, European Commission HORIZON 2020

Free Registration @ https://forms.gle/vCifjvCwTgCGrqJt8

For Further Queries, Please Contact

Dr. J. JAYANTHI (CONVENER)
DEAN RESEARCH, GNCR
researchdean@gurunanakcollege.edu.in

Dr. M. G. RAGUNATHAN
Principal

SARDAR MANJIT SINGH NAYAR
General Secretary & Correspondent

3. Photos


The Role of Transgenic fishes in Drug Discovery and the Scope for Entrepreneurship
Guru Nanak College
Webinar : October 01, 2020
Prof. Dr. S. G. PRAKASH VINCENT Ph.D (Indo-German)
DAAD Fellow (Germany)
EMBO Fellow (Germany)
UNESCO Fellowship Awardee (Italy)
MARIECURIE Fellow (European Commission)
Focal Point
European Commission HORIZON 2020
Chairman Associate (India)

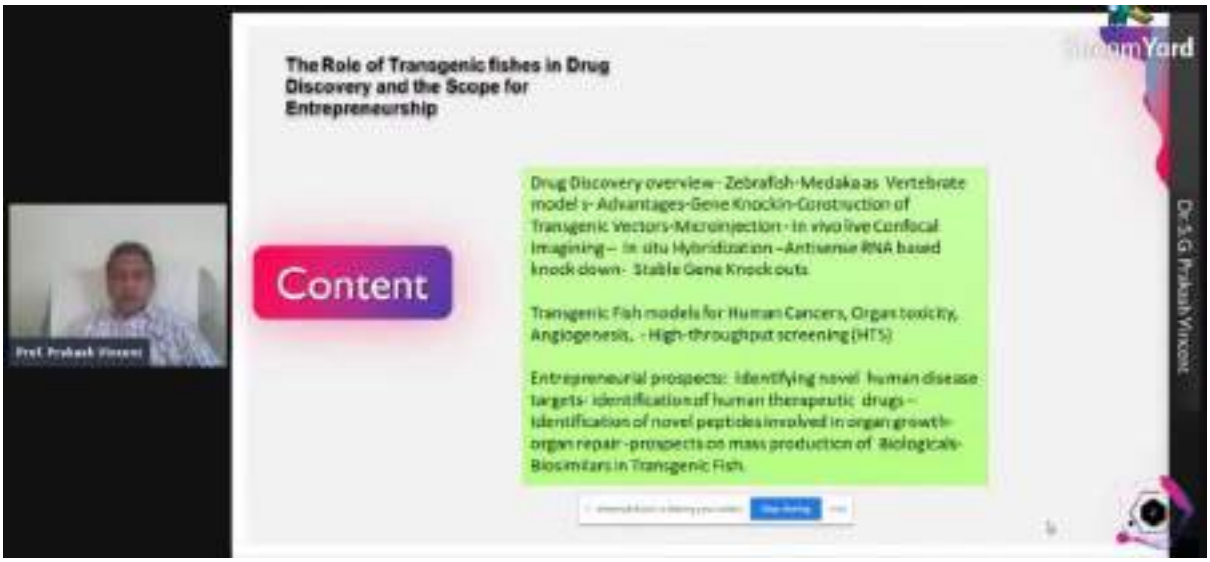

Dr. MAHENDRAKUMAR. M
Powered by StreamYard
Dr. L.R.S. Kalanithi, Vice Principal (SA)
Dr. J. Jayanthi - Dean Research
Prof. Prakash Vincent


StreamYard
Dr. L.R.S. Kalanithi, Vice Principal (SA)

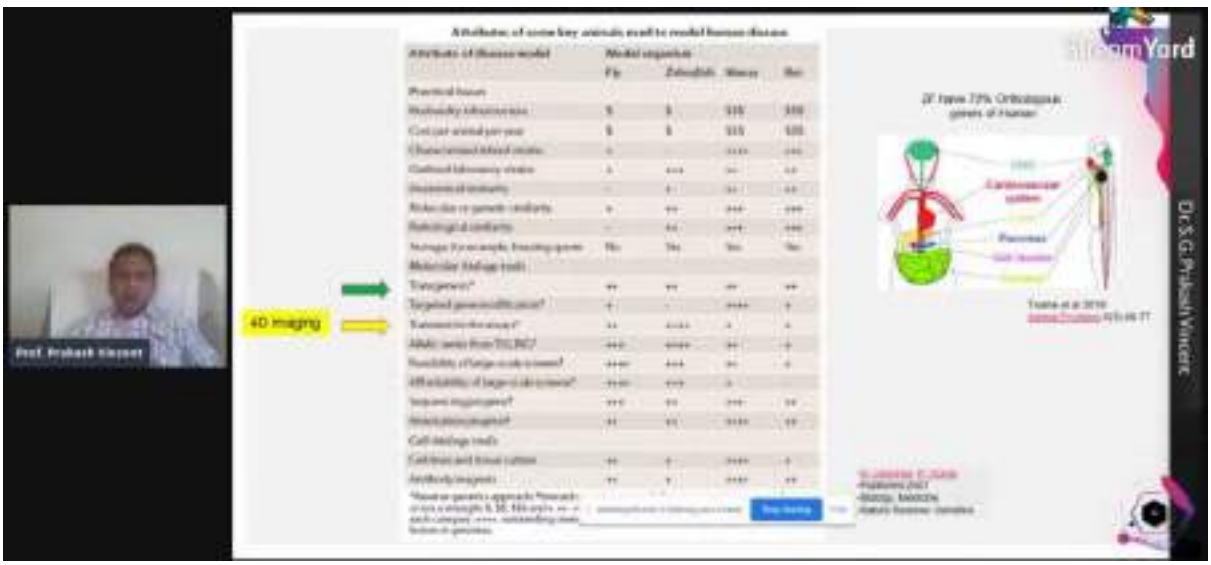

Dr. J. JAYANTHI, HOD - ZOOLOGY and DEAN RESEARCH

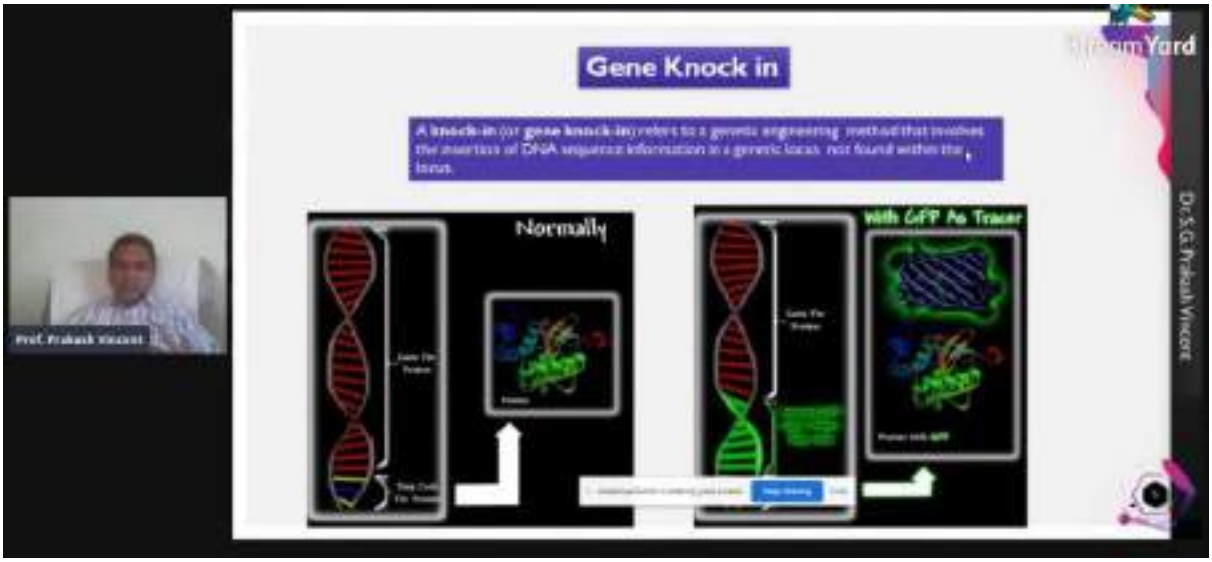

Dr. MAHENDRAKUMAR. M

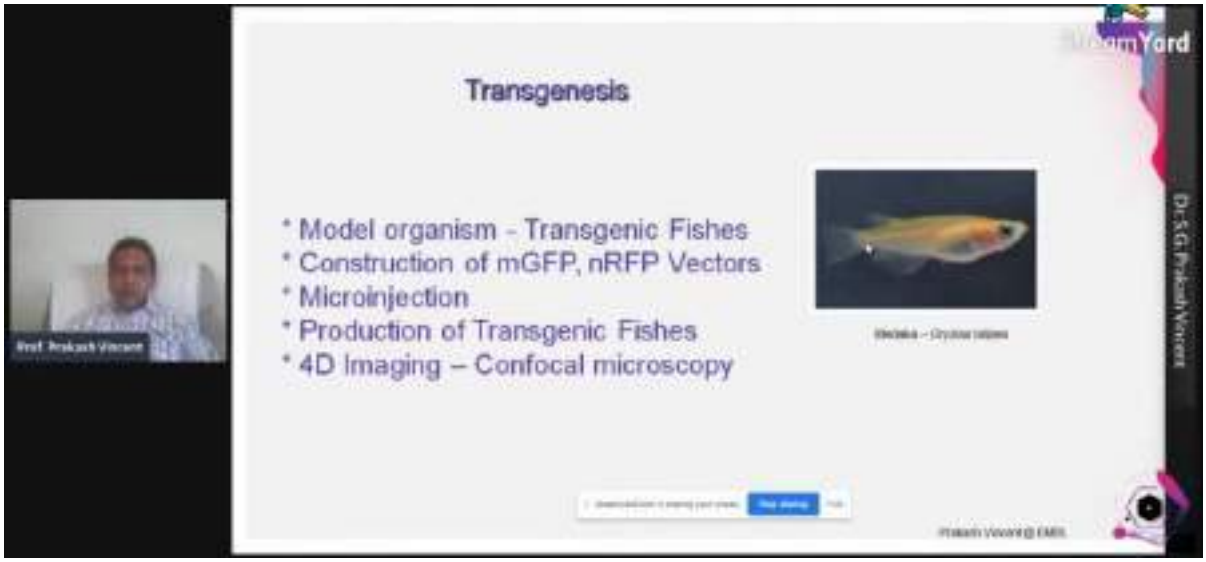

Prof. Prakash Vincent

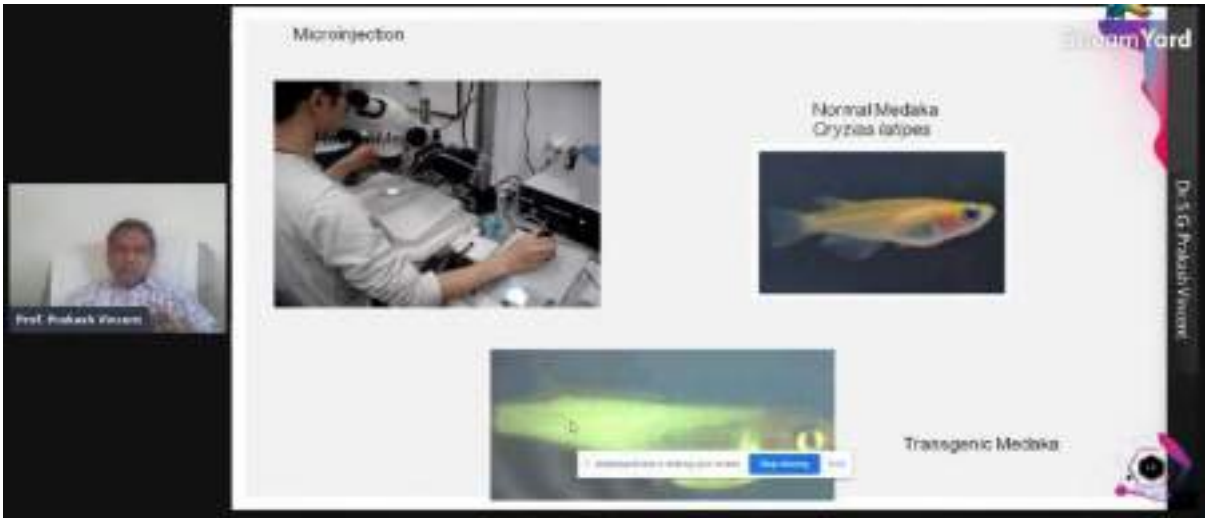

The Role of Transgenic fishes in Drug Discovery and the Scope for Entrepreneurship
Content
Drug Discovery overview- Zebrafish-Medaka as Vertebrate model s- Advantages-Gene Knockin-Construction of Transgenic Vectors-Microinjection - In vivo live Confocal Imaging – In situ Hybridization –Antisense RNA based knock down- Stable Gene Knock outs
Transgenic Fish models for Human Cancers, Organ toxicity, Angiogenesis, - High-throughput screening (HTS)
Entrepreneurial prospects: Identifying novel human disease targets- identification of human therapeutic drugs – identification of novel peptides involved in organ growth- organ repair -prospects on mass production of Biologicals- Biosimilars in Transgenic Fish
Prof. Prakash Vincent
Dr.S.G.Prakash Vincent
StreamYard

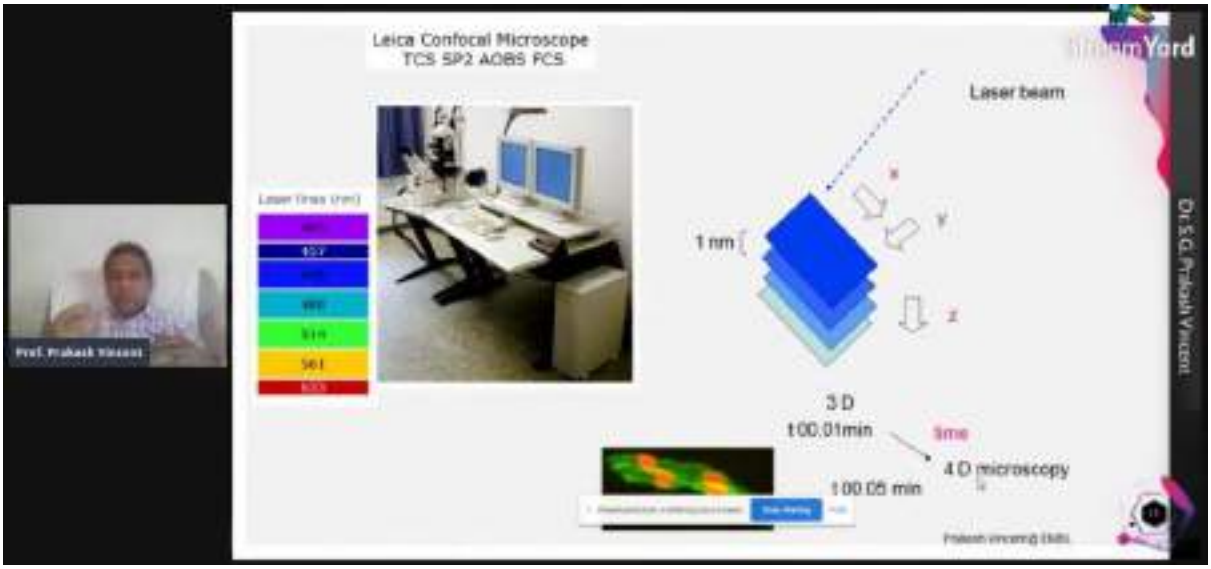

Drug Discovery Overview
15 years
1 drug Rs. 18000 crores
2.8 Billion USD
Danio rerio
Target
Hit/Lead
Prof. Prakash Vincent
Dr.S.G.Prakash Vincent
StreamYard

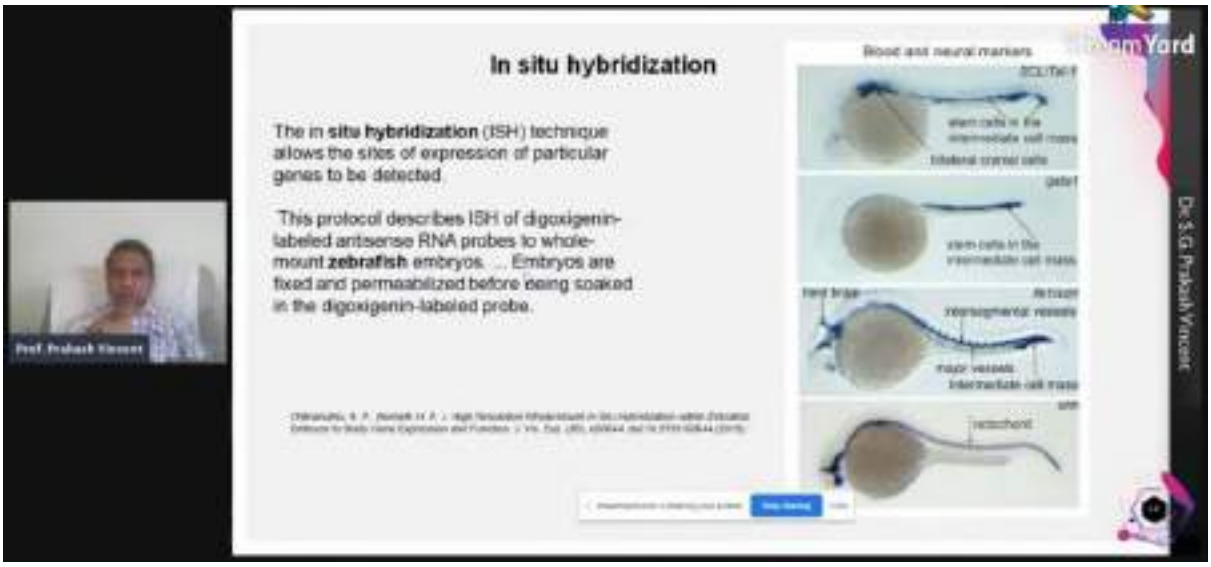

4D imaging
Prof. Prakash Vincent
Dr.S.G.Prakash Vincent
StreamYard

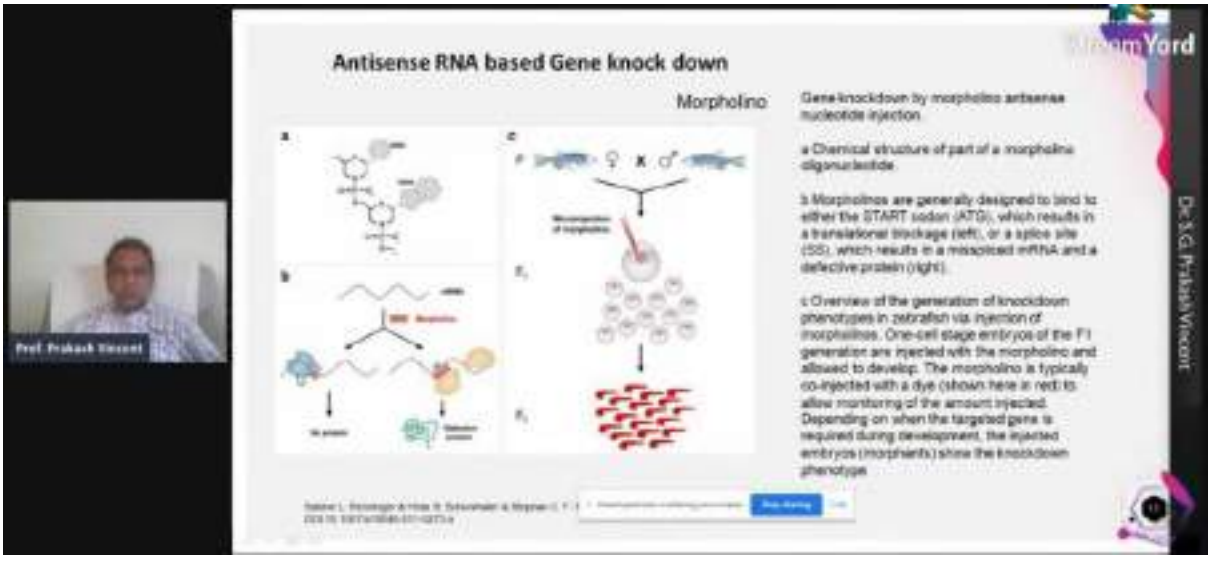

Gene Knock in
A knock-in (or gene knock-in) refers to a genetic engineering method that involves the insertion of DNA sequence information in a genetic locus not found within the locus.
Normally
With GFP As Tracer
Dr.S.G.Prakash Vincent

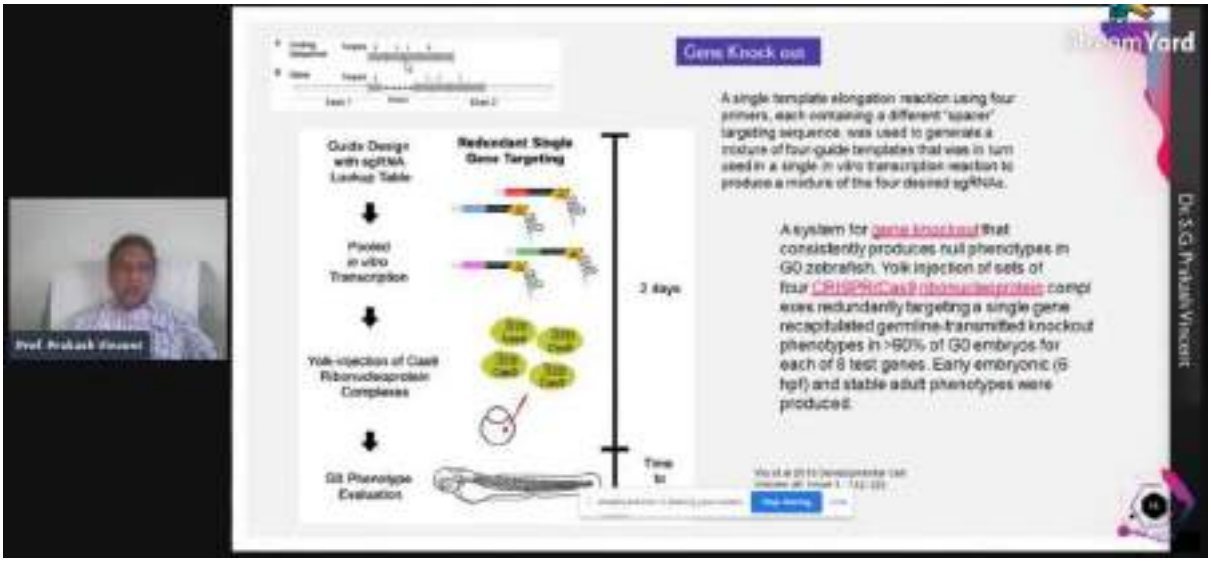

Transgenesis
* Model organism - Transgenic Fishes
* Construction of mGFP, nRFP Vectors
* Microinjection
* Production of Transgenic Fishes
* 4D Imaging – Confocal microscopy
Dr.S.G.Prakash Vincent

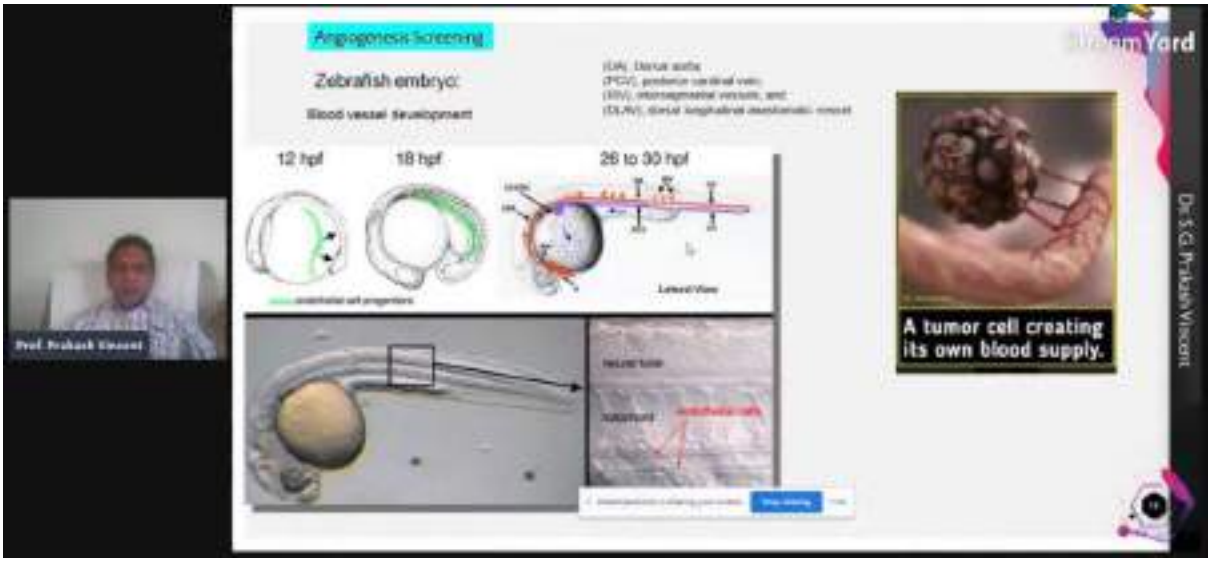

Microinjection
Normal Medaka
Oryzias latipes
Transgenic Medaka
Dr.S.G.Prakash Vincent

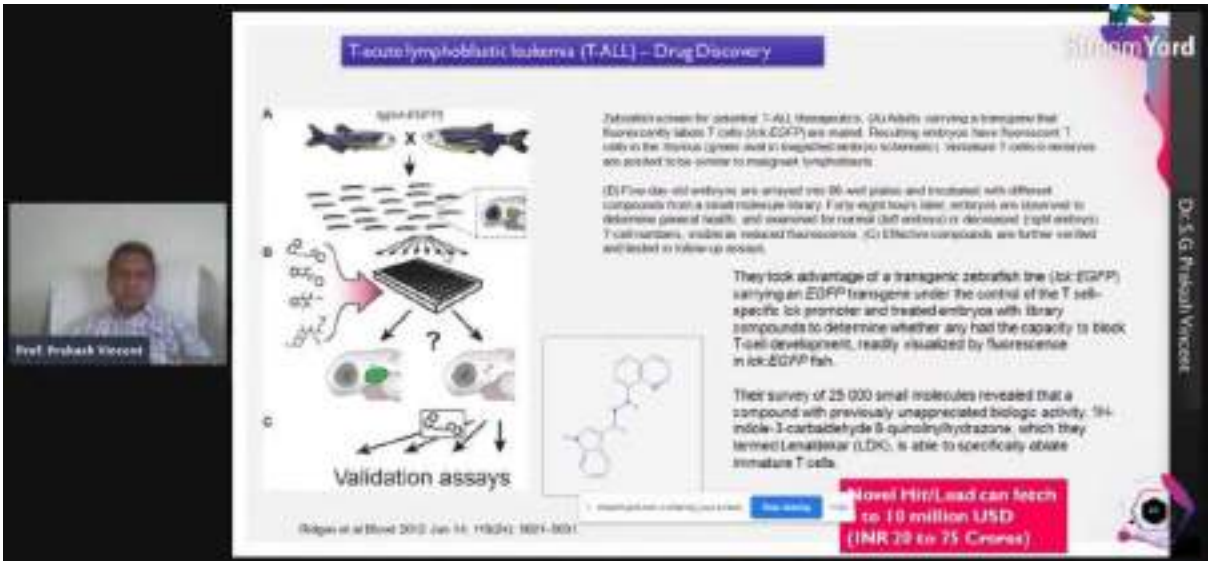

Leica Confocal Microscope
TCS SP2 AOBS FCS
Laser beam
1 nm
x
y
z
3 D
t 00.01min
time
4 D microscopy
t 00.05 min
Dr.S.G.Prakash Vincent

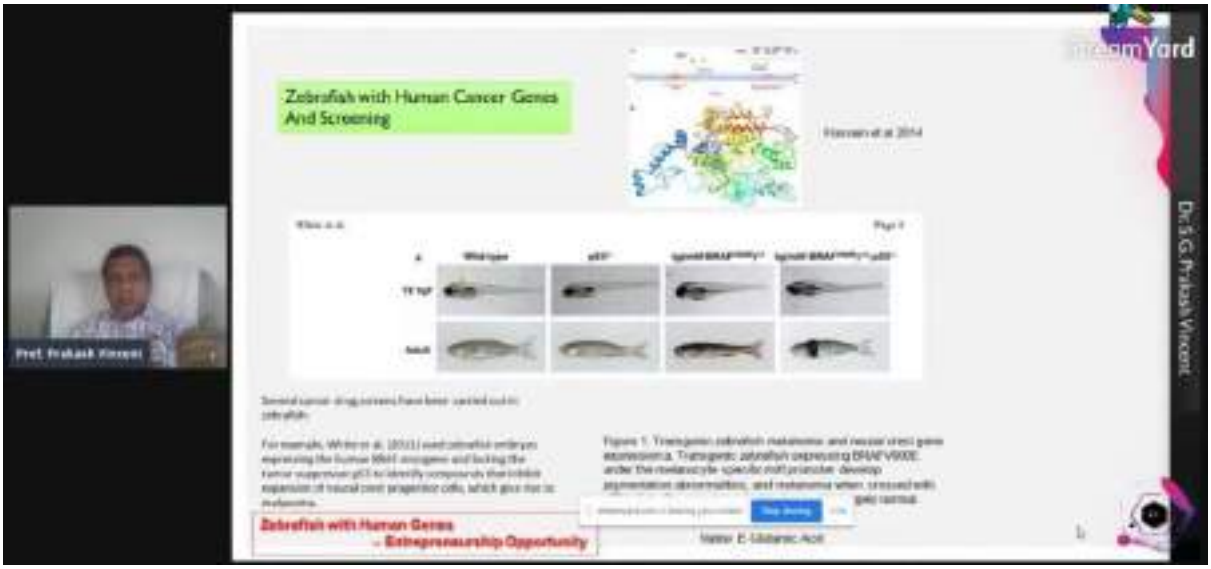

In situ hybridization
The in situ hybridization (ISH) technique allows the sites of expression of particular genes to be detected.
This protocol describes ISH of digoxigenin-labeled antisense RNA probes to whole-mount zebrafish embryos. ... Embryos are fixed and permeabilized before being soaked in the digoxigenin-labeled probe.
Blood and neural markers
Dr.S.G.Prakash Vincent

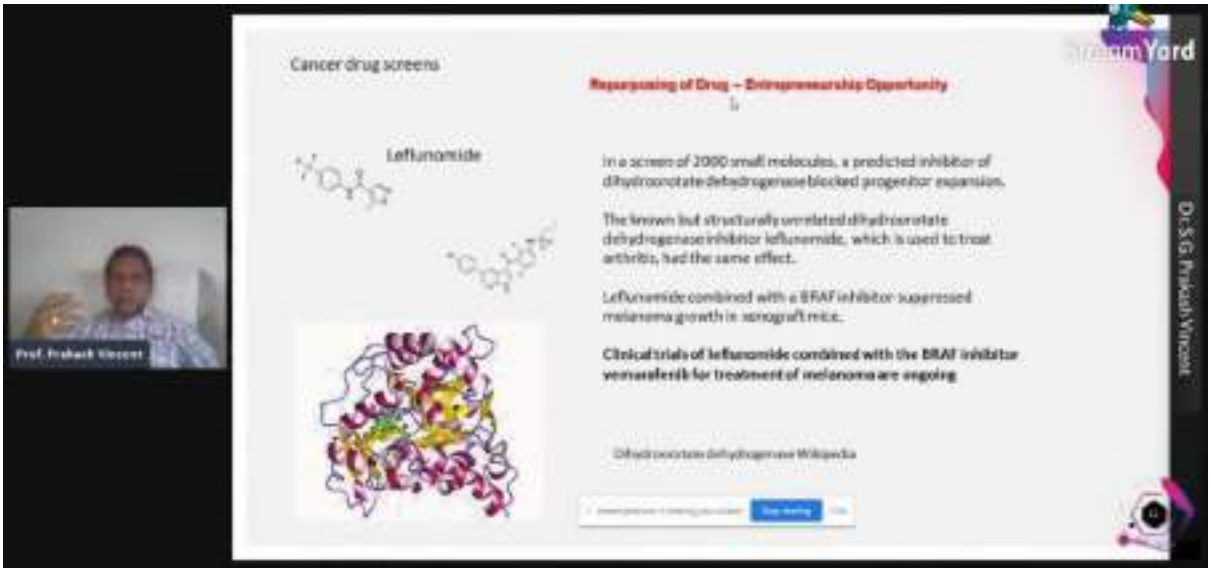

Antisense RNA based Gene knock down
Morpholino
Gene knockdown by morpholino antisense nucleotide injection
a Chemical structure of part of a morpholino oligonucleotide.
b Morpholinos are generally designed to bind to either the START codon (ATG), which results in a translational blockage (left), or a splice site (SS), which results in a misspliced mRNA and a defective protein (right).
c Overview of the generation of knockdown phenotypes in zebrafish via injection of morpholinos. One-cell stage embryos of the F1 generation are injected with the morpholino and allowed to develop. The morpholino is typically co-injected with a dye (shown here in red) to allow monitoring of the amount injected. Depending on when the targeted gene is required during development, the injected embryos (morphants) show the knockdown phenotype
Dr.S.G.Prakash Vincent

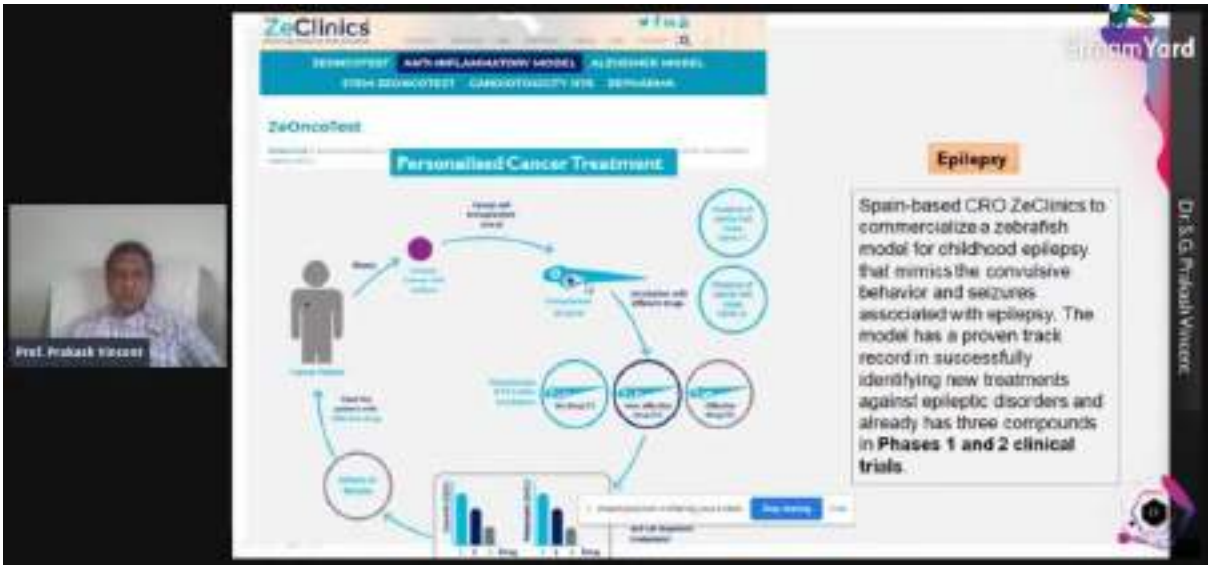

Gene Knock out
Guide Design with sgRNA Lookup Table
Pooled in vitro Transcription
Redundant Single Gene Targeting
3 days
Time to
G0 Phenotype Evaluation
A single template elongation reaction using four primers, each containing a different "spacer" targeting sequence, was used to generate a mixture of four guide templates that was in turn used in a single in vitro transcription reaction to produce a mixture of the four desired sgRNAs.
A system for gene knockout that consistently produces null phenotypes in G0 zebrafish. Yolk injection of sets of four CRISPR/Cas9 ribonucleoprotein complexes redundantly targeting a single gene recapitulated germline-transmitted knockout phenotypes in >80% of G0 embryos for each of 8 test genes. Early embryonic (6 hpf) and stable adult phenotypes were produced.
Prof. Prakash Vincent
Dr S G Prakash Vincent


Angiogenesis Screening
Zebrafish embryo:
Blood vessel development
12 hpf
18 hpf
26 to 30 hpf
A tumor cell creating its own blood supply.
Prof. Prakash Vincent
Dr S G Prakash Vincent


T-acute lymphoblastic leukemia (T-ALL) – Drug Discovery
Validation assays
They took advantage of a transgenic zebrafish line (lck:EGFP) carrying an EGFP transgene under the control of the T cell–specific lck promoter and treated embryos with library compounds to determine whether any had the capacity to block T-cell development, readily visualized by fluorescence in lck:EGFP fish.
Their survey of 25 000 small molecules revealed that a compound with previously unappreciated biologic activity, 9H-indole-3-carbaldehyde 9-quinolinylhydrazone, which they termed Lenaldekar (LDK), is able to specifically ablate immature T cells.
Novel Hit/Lead can fetch up to 10 million USD (INR 20 to 75 Crores)
Prof. Prakash Vincent
Dr S G Prakash Vincent


Zebrafish with Human Cancer Genes And Screening
Hanson et al 2014
Zebrafish with Human Genes – Entrepreneurship Opportunity
Dr S G Prakash Vincent


Cancer drug screens
Repurposing of Drug – Entrepreneurship Opportunity
Leflunomide
In a screen of 2000 small molecules, a predicted inhibitor of dihydroorotate dehydrogenase blocked progenitor expansion.
The known but structurally unrelated dihydroorotate dehydrogenase inhibitor leflunomide, which is used to treat arthritis, had the same effect.
Leflunomide combined with a BRAF inhibitor suppressed melanoma growth in xenograft mice.
Clinical trials of leflunomide combined with the BRAF inhibitor vemurafenib for treatment of melanoma are ongoing
Dr S G Prakash Vincent


ZeClinics
ZeOncoTest
Personalised Cancer Treatment
Epilepsy
Spain-based CRO ZeClinics to commercialize a zebrafish model for childhood epilepsy that mimics the convulsive behavior and seizures associated with epilepsy. The model has a proven track record in successfully identifying new treatments against epileptic disorders and already has three compounds in Phases 1 and 2 clinical trials.
Dr S G Prakash Vincent

Kidney regeneration

Reactivation of genes normally expressed during organogenesis is a characteristic of kidney regeneration. Enhancing this reactivation could potentially be a therapeutic target to augment kidney regeneration.

Kidney regeneration is characterized by dedifferentiation of surviving renal tubular epithelial cells into progenitor cells, associated with reactivation of genes normally required during organogenesis.12,13

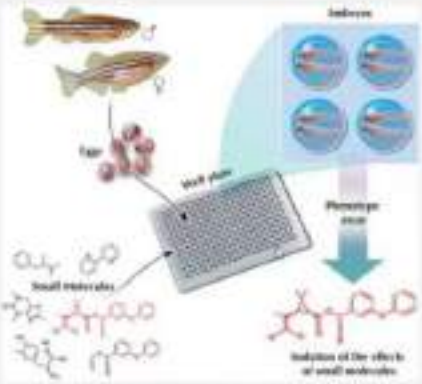
One of the genes reactivated during regeneration is the Lim homeobox protein, Lhx1 (formerly Lim1), which is essential during embryonic development for establishing the kidney field

Development of High-Content Assays for Kidney Progenitor Cell Expansion in Transgenic Zebrafish

UPHOLD

Subramaniam Sanker¹, Maria Cecilia Oliva¹, Laura L. Wallace¹, Benjamin Goldberg¹, Lee A. McDermott[2,3], Mark A. Hahnfeldt¹, and Andreas Vogt[1,4]

Cardioprotectant



One such example is highlighted on the right. A compound (SB2) identified in a zebrafish screen for suppressors of a plakoglobin mutant phenotype reduces the ventricular ectopic activity seen in a mouse model of the same desmosomal mutant protein.

In addition, the same compound rescues contractile abnormalities and conduction abnormalities observed in a mouse model of the related disorder caused by mutations in the desmoglein2 gene

Aaron Kilbourn, and Calum A. MacRae BTS 2017;2:1-12

JACC

Target Discovery

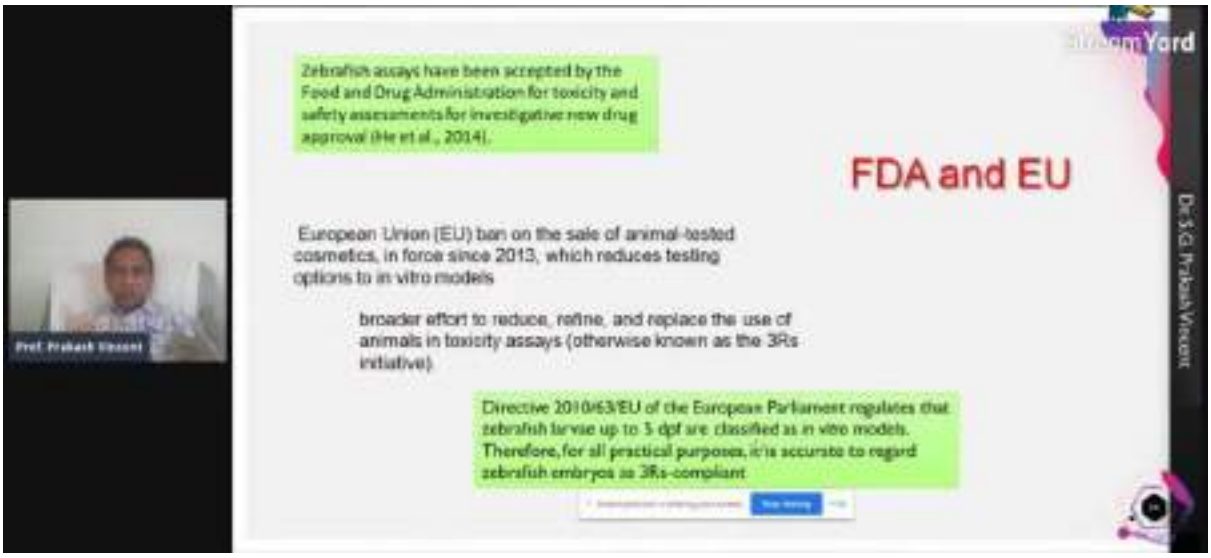
Novel Target could fetch 10 to 30 million USD (INR 75 to 225 Crores)

One of the most common cancers in children and adolescents is rhabdomyosarcoma, a cancer of soft tissue such as muscle, tendon or cartilage. The fusion of DNA on two different chromosomes causes the most aggressive form of rhabdomyosarcoma. The fused DNA produces an abnormal protein called PAX3-FOXO1.

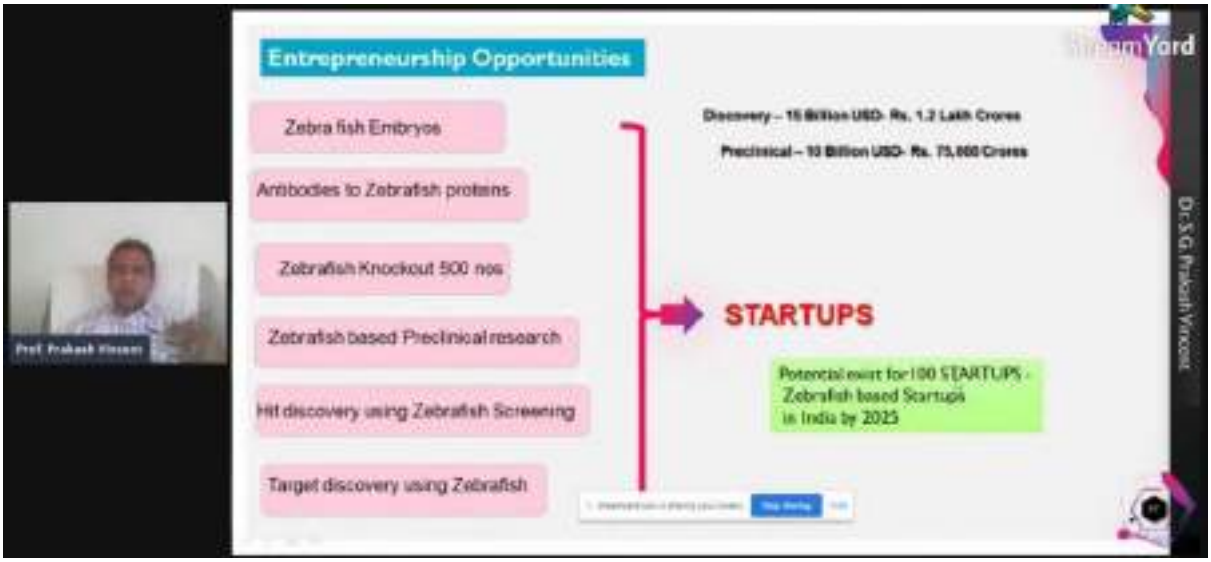
Iser3 is a novel developmental target of human PAX3-FOXO1

The PAX3/7-FOXO1 oncogenes remain intractable to therapeutic targeting, impeding the development of effective precision medicine therapies

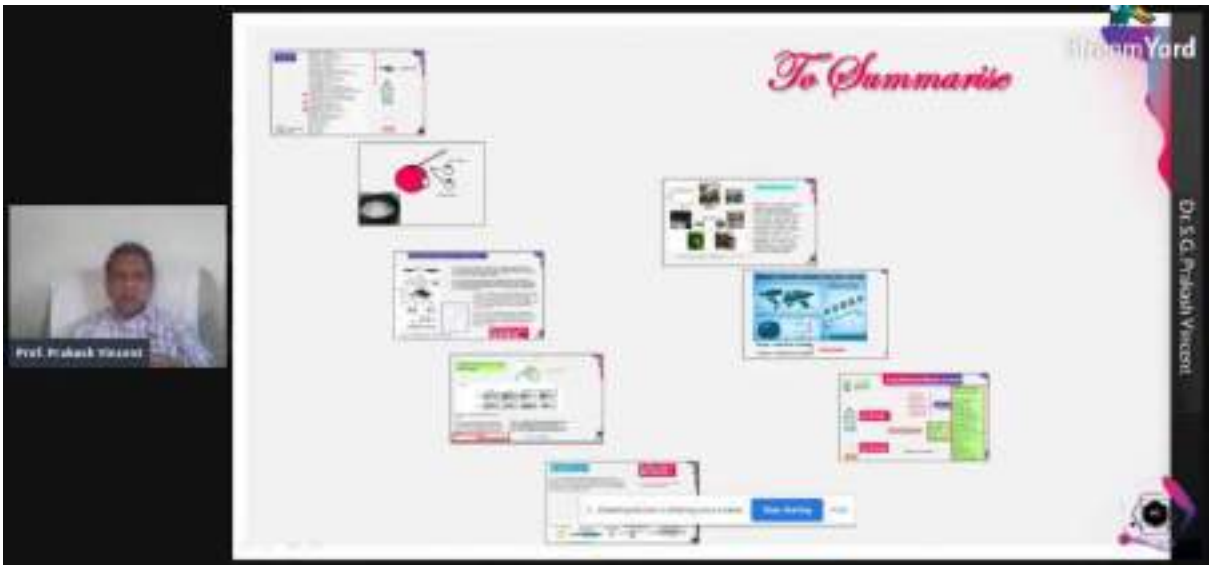

High-Throughput Screening
Zebrafish are an emerging vertebrate model for HT toxicity screening, disease modeling, phenotype discovery, and chemical mechanisms of action. Their high fecundity, low cost, and rapid development make nearly all in vivo biological assays amenable to HT studies. As assays and endpoints become more standardized with the use of modern technologies, the zebrafish has rapidly become one of the premier vertebrate models for biological discovery. HT high-throughput
Dr.S.G.PrakashVincent


Zebrafish assays have been accepted by the Food and Drug Administration for toxicity and safety assessments for investigative new drug approval (He et al., 2014).
FDA and EU
European Union (EU) ban on the sale of animal-tested cosmetics, in force since 2013, which reduces testing options to in vitro models
broader effort to reduce, refine, and replace the use of animals in toxicity assays (otherwise known as the 3Rs initiative).
Directive 2010/63/EU of the European Parliament regulates that zebrafish larvae up to 5 dpf are classified as in vitro models. Therefore, for all practical purposes, it is accurate to regard zebrafish embryos as 3Rs-compliant
Dr.S.G.PrakashVincent


CONTRACT RESEARCH ORGANIZATION (CRO) SERVICES
Global Contract Research Organization Services Market (US$ Mn), 2018 to 2028
Discovery – 15 Billion USD- Rs. 1.2 Lakh Crores
Preclinical – 10 Billion USD- Rs. 75,000 Crores
'S SPACE
Dr.S.G.PrakashVincent


Entrepreneurship Opportunities
Zebra fish Embryos
Antibodies to Zebrafish proteins
Zebrafish Knockout 500 nos
Zebrafish based Preclinical research
Hit discovery using Zebrafish Screening
Target discovery using Zebrafish
Discovery – 15 Billion USD- Rs. 1.2 Lakh Crores
Preclinical – 10 Billion USD- Rs. 75,000 Crores
STARTUPS
Potential exist for 100 STARTUPS - Zebrafish based Startups in India by 2025
StreamYard
Dr.S.G.Prakash Vincent


START UP INDIA
Drug Discovery Startups in India
Global Major Pharma out-licensing Clients
CROs for:
Target
Hit/Lead
StreamYard
Dr.S.G.Prakash Vincent


To Summarise
StreamYard
Dr.S.G.Prakash Vincent


SANGRAM KESHARI PANDA
Which drugs are already prepared by using the transgenic fishes & for which diseases ??


Manikandan B N
how to differentiate a normal fish from transgenic fish....what is the selectable markers used....for drug production in transgenic fish

4. Certificate Copy

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(AUTONOMOUS)

Affiliated to University of Madras & Re-accredited at 'A' Grade by NAAC

Guru Nanak Salai, Velachery, Chennai – 600 042.

GURU NANAK CENTRE FOR RESEARCH

NATIONAL WEBINAR ON

"THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP"

Certificate of Participation

This is to certify that

Dr. GEETANJALI RANA KANWAR

G. B. Pant University of Agriculture and Technology,

Pantnagar, Uttarakhand

has actively participated in the NATIONAL WEBINAR ON "THE ROLE OF TRANSGENIC FISHES IN DRUG DISCOVERY AND THE SCOPE FOR ENTREPRENEURSHIP" held on 01.10.2020 organized by the GURU NANAK CENTRE FOR RESEARCH (GNCR), GURU NANAK COLLEGE (AUTONOMOUS), Guru Nanak Salai, Velachery, Chennai – 600042.

Dr. J. JAYANTHI
DEAN RESEARCH & CONVENER

Dr. M. G. RAGUNATHAN
PRINCIPAL

SARDAR MANJIT SINGH NAYAR
GENERAL SECRETARY & CORRESPONDENT