# PHARMALOGOS

## DEPARTMENT OF PHARMACOLOGY - NEWS LETTER

An Official Publication of

**DEVAKI AMMA MEMORIAL COLLEGE OF PHARMACY**

*(Affiliated to Kerala University of Health Sciences, Thrissur and Approved by AICTE & PCI, New Delhi)*

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## ISSUE HIGHLIGHTS



## INSTITUTION VISION AND MISSION


To be the ultimate destination for training, practice and research in pharmacy education to cater the health needs of the society.


To provide state-of-art infrastructure, research facilities with eminent faculties to disseminate advanced knowledge in pharmacy education through innovative teaching- learning process with human and ethical values.

## CRISPR-Cas9 SCREENING IN PHARMACOLOGY

CRISPR-Cas9 is a powerful gene editing tool that cuts DNA in a precise, directed manner. CRISPR screening uses this technology to enable thousands of genes to be modified and their function assessed in a single experiment. This cutting-edge tool can help identify and validate novel drug targets or study the underlying causes of disease. It is also being used by researchers to identify the effect of genetic mutations on drug activity, patient responsiveness and resistance. As a fully integrated life science company, Horizon Discovery leads the way in offering a broad range of CRISPR screening services from initial design and cell-line selection to bioinformatics analysis of the screen results.

*In the remembrance of*

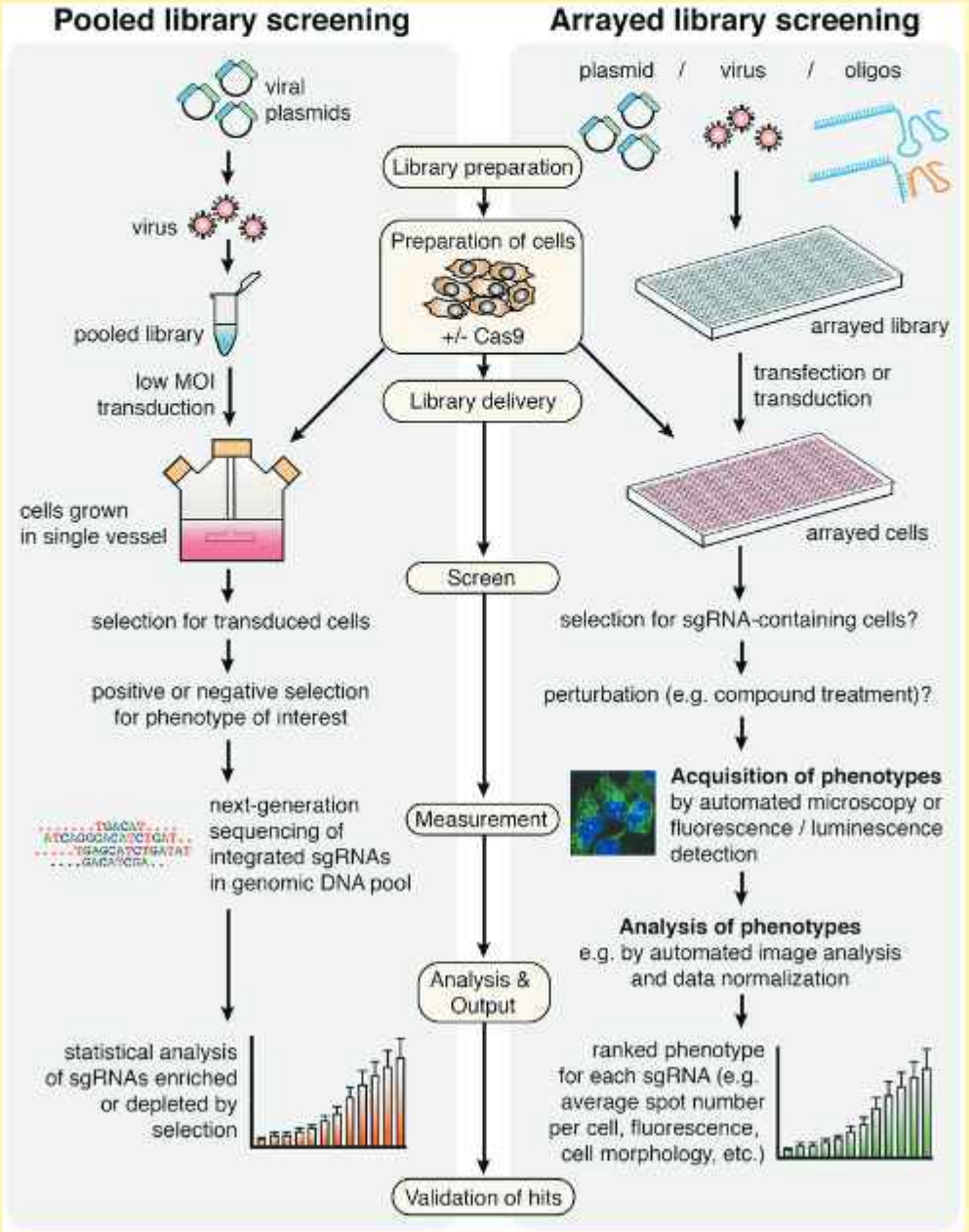
**Sri. K.V. Sankaranarayanan**

(01.01.1948 - 12.07.2013)

Founder, Devaki Amma Memorial Institutions

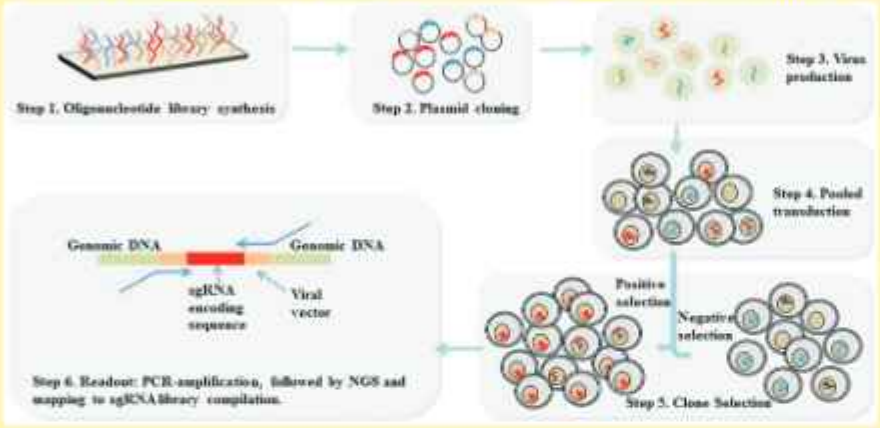
## CRISPR screening

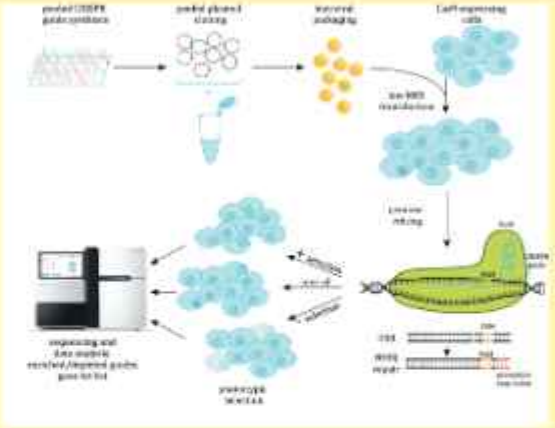
The CRISPR-Cas9 technology uses the Cas9 enzyme and guide RNA to edit the genome at a particular point. There are three different mechanisms we use: the most common is CRISPR KO (Knock Out) which completely inactivates a gene. The other two either activate (CRISPRa) or inhibit (CRISPRi) the expression of a gene without altering the DNA. CRISPR screening is an application of this technology, and we can do the screens in two ways. Our pooled format takes huge numbers of lentiviral guide RNAs and delivers them to a large population of cells. We can then select some of the cells and perturb them to look for a phenotypic effect - that is, to see which genes are providing a positive or a negative effect. The other way we screen is using an array, a 96-well or 384-well plate, to look systematically at individual genes or constructs. In this format we can the synthetic guide RNA to the cells and look for specific perturbations directly on a well-by-well basis.



## Steps involved in a CRISPR screening

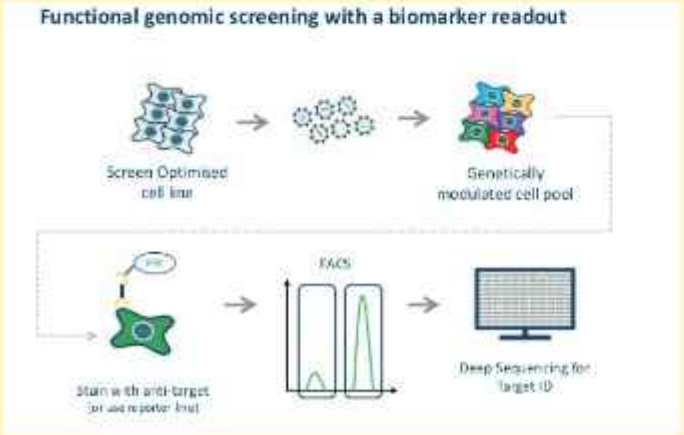
Steps involved in a CRISPR screen. First, the CRISPR plasmid library is amplified. Next, this library is packaged into lentivirus. Then Cas9-expressing cells are transduced with this virus. Mutant cells are screen and "hits" are identified using next-generation sequencing. Performing a forward genetic screen using CRISPR libraries is a multi-step process. In most cases, CRISPR libraries are provided at a concentration that is too low for experimental use. Thus, the first step is to amplify your library to a concentration that is sufficient to generate lentivirus. Be sure to use next-generation sequencing to check the quality of your amplication.

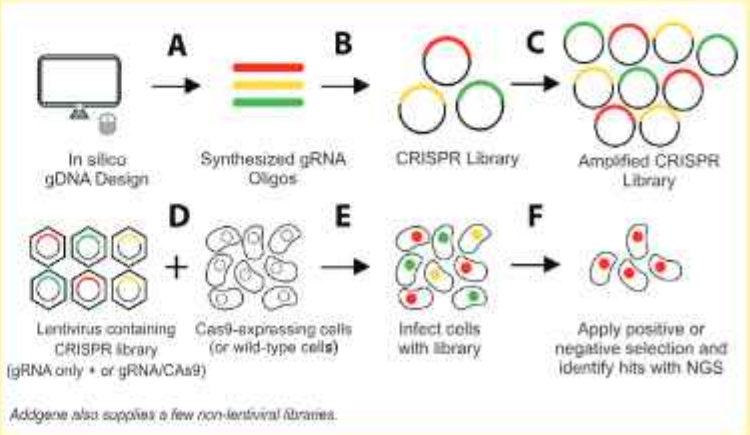


Cells are then transduced with lentivirus containing the CRISPR library to generate a heterogeneous population of mutant cells, with each cell or set of cells containing a mutation in a different gene. Libraries may be available in a 1-plasmid system, in which Cas9 is included on the gRNA-containing plasmid, or a 2-plasmid system in which Cas9 must be delivered separately.

Mutant cells are enriched using either drug selection or fluorescence-based cell sorting and screened for a particular phenotype. For example, mutant cells can be used in drug screens to identify genes that confer drug-resistance. Here, mutant cells are treated with a drug of interest and gRNA distribution is analyzed in the drug-resistant population compared to a non-treated control group. In this scenario, gRNAs that are "enriched" correspond to genes that confer drug resistance when mutated. Findings from this type of experiment can shed light on the mechanism by which cells gain resistance to drugs and can identify future therapeutic targets for diseases causing uncontrolled cell growth, such as cancer.



**Considerations and tips for successful screens**

- Next-generation sequencing - CRISPR libraries contain thousands of gRNA plasmids, discerned only by a unique barcode on each plasmid. As such, sequencing CRISPR libraries after amplification and after a screen requires the use of next-generation sequencing.
- Representation - Most libraries contain 3-6 gRNAs per target gene, and maintaining the distribution of each gRNA within the population is key. Loss of representation due to enrichment or depletion of specific gRNAs can lead to skewed results.
- Selecting a cell type - Theoretically, any cell type can be used in a CRISPR screen. However, maintaining sufficient representation within your mutant population requires a massive amount of cells as starting material. Therefore, cell types that are of low abundance are not particularly well suited for genome-wide screening.
- Avoid false positives and false negatives - As with any experiment, the use of appropriate controls, multiple replicates and several cell types can strengthen your results. Enrichment or depletion of multiple gRNAs targeting the same gene can be strong evidence that a particular gene is actually important for a given phenotype. Each hit from the screen should be independently validated to ensure that the desired modification produces the phenotype you screened for in the first place.
- With the proper experimental design and validation practices, CRISPR libraries can help you learn a lot about your phenotype of interest. To learn a bit about how CRISPR/Cas9 can be used in other types of experiments, check out our CRISPR Plasmids and Resources Page.

**Advantages of CRISPR screening**

Compared with older technologies such as RNA interference, CRISPR screening has greater specificity to its genomic target, which means we can get a much cleaner signal. Further, we are able to view the effects of complete gene knockout rather than partial reduction. With CRISPRi and CRISPRa we can target the endogenous gene at the transcriptional start site. This allows us to modify the expression of the gene in the cellular state, so we get more biological context. The speed with which CRISPR has enhanced therapeutic development is astronomical. It has enabled researchers to very quickly identify specific genes that are relevant to a specific biological pathway. In an applied setting, such as during preclinical development, researchers can more quickly identify compounds that will be successful in clinical trials or more easily identify ideal candidate patients or those to exclude, reducing the risk of late state trial failure.

**Applications of CRISPR screening**

One of the biggest therapeutic advantages is in personalized medicine. If one can determine which genes promote or reduce the activity of a particular therapeutic compound, you can stratify a patient population. In other words, if someone has a particular gene, you can give them targeted therapeutics that will ultimately be more effective - rather than going broader spectrum and playing the odds. However, it's not just drugs. There is also significant interest in using this technology in cell engineering. For instance; can we find the genes responsible for particular cell behaviour such as differentiation, or alternatively can we make an engineered T-cell and use that to hunt and destroy a cancer cell without harming healthy tissue.

**Benefit to the customer of Horizon's CRISPR screening services**

Among the biggest benefits are time and resources, by allowing us to help with the time-consuming screening work, this allows researchers to focus on the more critical questions and takes in their research. Our breadth of platforms enables us to design custom solutions to almost any screening requirement and cellular background. When coupled with our larger portfolio of reagents and services, we can more efficiently help researchers navigate to a successful therapeutic development. We work with everyone from very small start-up biotechs that may focus on only one or two specific targets, up to the biggest biopharma companies. Because of the breadth of our capability and our extensive experience we can tailor ourselves to be an extension of a company's own research facilities.

**Ms. Aiswarya Babu K**
**III Sem. M. Pharm**

## FDA APPROVED DRUGS IN PAST 6 MONTHS


The following database contains a list of new drugs approved by Food and Drug Administration (FDA) for sale in the United States. Drug information is as follows.

| BRAND NAME | DRUG | MANUFACTURER | TREATMENT | APPROVED MONTH |
|---|---|---|---|---|
| Pexidartinib | Turalio | Daiichi Sankyo company | Tenosynovial Giant cell tumor | August 2019 |
| Pitolisant | Wakix | Harmony Biosciences | Narcolepsy | August 2019 |
| Lefamulin | Xenleta | Nabriva therapeutics | Community acquired bacterial pneumonia | August 2019 |
| Ibsrela | Tenapanor | Ardelyx | Irritable bowel syndrome with constipation | September 2019 |
| Brolucizumab | Beovu | ESBA Tech | wet age-related macular degeneration | October 2019 |
| Lasmiditan | Reyvow | Elililly | migraine | October 2019 |
| Luspatercept-aamt | Reblozyl | Accelerone Pharma | Anemia in adult patients with beta thalassemia | November 2019 |
| Cenobamate | Xcopri | SK Pharmaceuticals | Partial onset seizures | November 2019 |
| Voxelotor | Oxbryta | Global blood Therapeuticals | Sickle cell disease | November 2019 |
| Golodirsen | Vyondys 53 | Sarepta therapeutics | Duchenne muscular dystrophy | December 2019 |
| Brilliant Blue G Ophthalmic Solution | Tissue Blue | Optitech | Dye in Eye surgery | December 2019 |
| Fam-trastuzumab deruxtecan-nxki | Enhertu | Astrazeneca & daiichi sankyo | Breast cancer | December 2019 |

**Mrs. Mumthaz P**
**III Sem. M. Pharm.**

## DEPARTMENT HIGHLIGHTS

### PAPER PUBLICATIONS

- Suresh Arumugam, Sneha Prakash, Sreerag Azhakath, Lydia Abraham, Lakshmi Prakashan, Anusree Anaparakkal. Interventional Study Based on Prescription Errors in the Inpatient Units of a Tertiary Care Hospital in Calicut. Indian Journal of Pharmacy Practice. 2019; 12(4): 229-233.
- Venkatesh S and Sreelakshmi S.S. Anti-snake venom activity of the leaves and stem bark extract of *Alstonia venenata* R.Br. by *in-vitro* and *in-vivo* methods in Swiss albino mice. Journal of Pharmacy and Pharmacology. 2019; 1(6): 153-159.
- Prajitha P, Suresh A, Deepak VS, Hiba Faslu. *A Review on Epiphyllum oxypetalum* (DC) Haw. Asian Journal of Research in Chemistry and Pharmaceutical Sciences. 2019; 7(3): 824-830.
- Sellamuthu Venkatesh, Angappan Sheela. Anti-venom activity of *ethanolic extract of leaves of Ampelocis susaraneosa*. International Journal of Pharmaceutical Research. 2019; 11(1): 719-724.
- Deepak VS, Suresh A, Amritha CK, Prajitha P, Hiba Faslu. Phytopharmacological Activities of *Ludwigia hyssopifolia* (G.Don) Exell: Review. Asian Journal of Research in Chemistry and Pharmaceutical Sciences. 2019; 7(2): 781-789.
- Sreelakshmi SS, Venkatesh S. A Review on Phyto-pharmacological profile on *Alstonia venenata* R.Br. American Journal of Pharmtech Research.2019; 9 (2):64-73.

### INTERNATIONAL CONFERENCE

Mr. Mridhul Mohan, Asst. Professor, First and Third semester M. Pharm. Pharmacology students attended an International Conference on "DYANAMIC APPROACHES AND ROBUST SOURCES INTO THE EVOLVING ROLE OF NATURAL PRODUCTS AS NEW DRUG LEADS" organized by Nandha College of Pharmacy, Erode, Tamilnadu on 16th & 17th December, 2019.

## NATIONAL SEMINAR AND WORKSHOP

Dr. E. Tamil jothi, Associate Professor and Mr. S. Venkatesh, Assistant Professor attended workshop on "ORGANZA - Favour to Society Palliative care" organized by Devaki Amma Teacher Education Institute, Chelembra, Malappuram on 5th January, 2020.


Mohamed Shibli PC, Jincy TC, Anjitha P, Asheena Asharaf VV, Anaswara R Nath, Aswathi K, Anju Susanna Alex and Hashly Parveen of first Semester M. Pharm. (Pharmacology) students attended "5th NATIONAL SYMPOSIUM CUM WORKSHOP ON EXPERIMENTAL RESEARCH & ALTERNATIVES (NSWERA) organized by Department of Pharmacology, Amrita Institute of Medical Sciences, Kochi on 1st & 2nd November, 2019.

## SCIENCE EXHIBITION

Mrs. Bhavya Sivadas P, Asst. Professor and First semester M.Pharm. Students conducted a part of Science Exhibition, "DHYUTHI 2019" at Feroke Higher Secondary School, Farook College Campus, Feroke and Narayanan Nair Memorial Higher Secondary School, Chelembra on 1st October, 2019.

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