



PHARMALOGOS

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Website: www.devakiammamemorial.org E-mail: devakiammapharmacycollege@gmail.com

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ISSUE HIGHLIGHTS

- ☛ Transgenic Animals and their Applications in Medicine
- ☛ FDA Approved drugs in Past Five Months

Transgenic Animals and their Applications in Medicine

Transgenic animals are animals that are genetically altered to have traits that mimic symptoms of specific human pathologies. They provide genetic models of various human diseases which are important in understanding disease and developing new targets. Various aspects of concern in the coming years are the regulatory guidelines, ethical issues and patents related to the use of transgenic animals. This modern medicine is on the threshold of a pharmacological revolution. Use of transgenic animals will provide solutions for drug research, xenotransplantation, clinical trials and will prove to be a new insight in drug development.

An animal model is a living, non-human animal used for research and investigation of human disease, for the purpose of better understanding the disease without the added risk of causing harm to a human being during the entire drug discovery and development process. Transgenic animal models are created by the insertion of a particular human DNA into fertilized oocytes which are then allowed to develop to term by implantation into the oviducts of pseudo pregnant females. There are different models of transgenic animals for various diseases.

Making of Transgenic Animals

There are three types of laboratory animal models; they are spontaneous, induced and transgenic. Spontaneous models shape up as a result of naturally occurring mutations. Induced models are produced by a laboratory procedure like administration of a drug or chemicals, feeding of special diets or surgical procedure. The third category includes



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transgenic models. Transgenic refers to insertion of cDNA made from specific mRNA into cells. A transgenic animal is defined as an animal which is altered by the introduction of recombinant DNA through human intervention.

A. Human Immuno Virus/ Acquired Immuno Deficiency Syndrome (HIV/AIDS)

Tg26 HIVAN Mouse Model was the first transgenic model developed in 1991 for HIV. These transgenic animals can express HIV-1 proteins; develop symptoms and immune deficiencies similar to the manifestations of AIDS in humans. Other models are AIDS Mouse, Cotton rat and Smart Mouse. Cotton rat is susceptible to a wide range of human infectious disease agents, Respiratory Syncytial Virus, Herpes Simplex (Type 1 & Type 2), Para influenza Type 3, Polio, Measles, Monkeypox, Metapneumo virus, Human Immunodeficiency Virus and Influenza Virus.



Cotton Rat



ApoE knockout Mouse



Diabetic Zucker Rat

B. Alzheimer's disease

No animal models existed for the disease before transgenic technology was employed. Immunization of Amyloid precursor protein A42 in transgenic mice showed that vaccination against Alzheimer's disease could have potential as a therapeutic approach. Different animal models like Alzheimer's mouse amyloid pathology mouse models (PDAPP mice and Tg2576 mice) TAU transgenic mouse models (ALZ7 mice, TauTg mice) and presenilin transgenic models (ApoE knockout) are developed to study Alzheimer's disease.

C. Cardiovascular disease

Various transgenic animal models for gain and or loss of function of angiotensin, endothelin, natriuretic peptides, catechoalmines, Calcium binding-signaling, sodium channel transporters, and nitric oxide synthesis involved in cardiovascular regulation are used to study cardiovascular diseases. Mutation of the ApoE gene that is critical for uptake of chylomicrons and very low density lipoprotein particles, results in a model that develops atherosclerotic lesions histologically similar to those found in humans.

D. Diabetes Mellitus

Transgenic models are developed for studying the genes, and their role in peripheral insulin action. Models of insulin secretion such as glucokinase, islet amyloid polypeptide, and hepatic glucose production in type 2 diabetes are developed. A transgenic mouse model that expressed Insulin Dependent Diabetes Mellitus by inserting a viral gene in the animal egg stage is also developed. There are other models like Beta receptor knockout mouse, Uncoupling Protein (UCP1) knockout mouse, Diabetic Zucker rat, acute and chronic models for the evaluation of antidiabetic agents.

E. Cancer disease

Oncomouse was first transgenic animal to be patented. Its germ cells and somatic cells contain an activated human oncogene sequence introduced into the animal at an early embryonic stage to ensure that the oncogene is present in all the animal cells. Transgenic animal models are used in the assessment of mutagenicity, carcinogenicity and tools for understanding metabolic enzymes and receptors. There are transgenic animal models for mutagenicity assays approved by the WHO like LACI transgenic model and LACZ transgenic model. BALB/c mice are useful for research into both cancer and immunology.



BALB/c mice



C57BL/6



Long Evans hooded

F. Behavioral and obesity research

Long - Evans hooded

This genetic animal developed by crossing Wistar females with wild gray male. Colour of head and extremities is black or brown. Rest of the body is white with pigmented eyes. It can be easily handled and level of aggressive behavior is generally high.

Zucker rats

They have faulty leptin receptors. Leptin can't bind to the faulty receptor, so Zucker rats never feel full. They eat constantly and become morbidly obese. So they are used as models for obesity, diabetes and heart disease.

Transgenic Animal Applications

A representative, but non-inclusive, list of purposes for which transgenic animals have been used indicates the wide ranging application of this biotechnology:

- Medical research, transgenic animals are used to identify the functions of specific factors in complex homeostatic systems in toxicology:
- Mammalian developmental genetics.
- Molecular biology, the analysis of the regulation of gene expression.
- Pharmaceutical industry, targeted production of pharmaceutical proteins, drug production and product efficacy testing.
- Biotechnology: as producers of specific proteins and xenografting.

Mrs. Rafa Zubair
II M.Pharm

FDA Approved Drugs in past Five Months

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



DRUG	BRAND NAME	MANUFACTURER	TREATMENT	APPROVED MONTH
Baricitinib	Olumiant	EliLilly	Rheumatoid arthritis	May 2018
Erenumab	Aimovig	Amgen	Preventive treatment of migraine in adults	May 2018
Avatrombopag	Doptelet	AkaRx	Treatment of thrombocytopenia in adults with chronic liver disease	May 2018
Sodium Zirconium Cyclosilicate	Lokelma	AstraZeneca	Treatment of hyperkalemia	May 2018
Lofexidine	Lucemyra	US Worldmeds	Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults.	May 2018
Tolvaptan	Jynarque	Otsuka America	Polycystic Kidney Disease	April 2018
Fostamatinib Disodium Hexahydrate	Tavalisse	Rigel Pharmaceuticals.	Idiopathic (Immune) Thrombocytopenic Purpura	April 2018
Burosumab	Crysvita	Ultragenyx	Musculoskeletal Diseases (X- linked hypophosphatemia)	April 2018
Tildrakizumab	Ilumya	Sun Pharmaceuticals	For the treatment of plaque psoriasis	March 2018

DRUG	BRAND NAME	MANUFACTURER	TREATMENT	APPROVED MONTH
Ibalizumab-uiyk	Trogarzo	Taimed Biologics	To treat HIV patients who have limited treatment options	March 2018
Apalutamide	Erleada	Janssen Biotech	Prostate cancer	February 2018
Tezacaftor/ Ivacaftor	Symdeko	Vertex	Cystic fibrosis	February 2018
Bictegravir/ Emtricitabine/ Tenofovir alafenamide	Biktarvy	Gilead	HIV-1 infection in adults	February 2018
Lutetium Lu 177 dotatate	Lutathera	Advanced Accelerator Applications	Gastroenteropancreatic neuroendocrine tumors	January 2018

Ms. Anupam Prahlad
H M.Pharm

DEPARTMENT HIGHLIGHTS

Workshop Conducted

One day workshop on the title "Ethics of Animal Handling and Blood Sampling of Laboratory Animals" was organized by Department of Pharmacology, on 22nd February, 2018. Dr. K. P. Sreekumar, Professor in Research Co-ordination and Director of International Co-operation and Initiatives, Kerala Veterinary and Animal Sciences University, Mannuthy, Thrissur, and Dr. Bibu John Kariyil, Assistant Professor, Department of Veterinary Pharmacology and Toxicology, Kerala Veterinary and Animal Sciences University, Mannuthy, Thrissur, were the speakers and demonstrators.



Inaugural Ceremony



Welcome Address by
Dr. A. Suresh, Professor & Head, Dept. of Pharmacology



Dr. K. P. Sreekumar delivered his talk on
"Ethical Research"



Dr. Bibu John Kariyil delivered his talk on
"Biomethodology in Laboratory Animal Management"



Feedback given by a Delegate



Vote of Thanks given by Mr. S. Venkatesh,
Asst. Professor, Dept. of Pharmacology

Seminar/ Conferences Attended

Our faculties and PG students were sponsored to take part as a delegate in National conferences to update the current trends and developments in our field. The below mentioned seminars and conferences attended by our faculties and students.



National Seminar at St. James College of Pharmaceutical sciences, Chalakkudy



National Seminar at Al Shifa College of Pharmacy, Perinthalmanna

Research Activities

The institute is inspired by identifying future needs of human resources to be felt by fast developing academic and scientific research in the area of Pharmacology. The following research activities are ongoing in the Department of Pharmacology.

- Anti Cancer activity in different cell lines.
- NSAID drugs and CCl₄ induced Hepatotoxicity study.
- Anti Diabetic activity of Streptozotocin induced model.
- Anti Anemic activity of Pentylenetetrazole induced model.
- Anti Spasmodic activity.
- Analgesic and anti Inflammatory activity.
- Anti Arthritic activity.
- Anti Depressant activity.
- Toxicity studies.
- Bioavailability and Skin irritation study.

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