pharmahorizon

A panorama in the world of health sciences

NEWSLETTER FROM DEPARTMENT OF PHARMACY, SUMANDEEP VIDYAPEETH | OCT-DEC 2017 I Vol III Issue 4

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EDITOR-IN-CHIEF'S VIEW:

It gives me great privilege to write the editorial of the present issue of "Pharmaporizon". We have been successsfully publishing this Newsletter for the past three years. However, we could not come out with two issues due to unavoidable circumstances. From 2018 onwards "Pharmahorizon" will be half yearly and it will have a new facelift. In the future editions articles from eminent personalities of pharmaceutical industries, doctors, information regarding sports medicines, case reports and alumni news etc will be incorporated. In this issue, a tribute to a Japanese scientist Yoshinori Ohsumi for his discovery on autophagy has been bestowed. We also try to disseminate a recent study on the effective treatment of Chronic Kidney Disease (CKD) with a small molecule (AC1903). A write up on regulatory changes in India on clinical trials, new drug approval for shock conditions, treatment of impetigo, drugs in the clinical trials and new molecule entity are some of the salient features of this newsletter. A study carried out at Cardiff University found that Niclosamide, an old drug for the treatment of tapeworm has been shown to be effective in Parkinsonism - An old wine in the new bottle. In this issue, we congratulate our faculty for their national awards and a sense of appreciation to our students who have successfully conducted several events. The editorial board wish all the readers a Happy 2018.

Dr. R Balaraman, Ph.D, FAMS, FIPS

A tribute to Discoverer of Autophagy Nobel Prize: 2016

Yoshinori Ohsumi

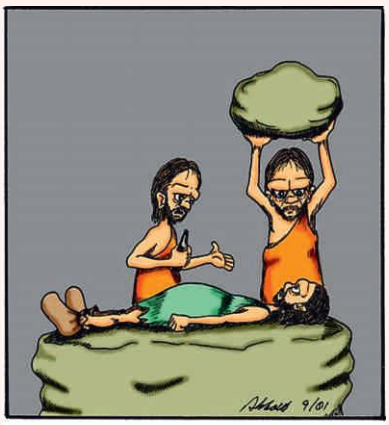
Yoshinori Ohsumi (born February 9, 1945) is a Japanese cell biologist specializing in 'autophagy'. Ohsumi is a Professor at Tokyo Institute of Technology's Institute of Innovative Research. He received the Kyoto Prize for Basic Sciences in 2012, the 2016 Nobel Prize in Physiology or Medicine, and the 2017 Breakthrough Prize in Life Sciences for his discoveries of mechanisms for autophagy.

Autophagy is a fundamental process for degrading and recycling cellular components. Autophagy denotes "self eating". This concept emerged during the 1960's, when researchers first observed that the cell could destroy its own contents by enclosing it in membranes, forming sack-like vesicles that were transported to a recycling compartment, called the lysosome, for degradation. Difficulties in studying the phenomenon meant that little was known until, in a series of brilliant experiments in the early 1990's, Yoshinori Ohsumi used baker's yeast to identify genes essential for autophagy. He then went on to elucidate the underlying mechanisms for autophagy in yeast and showed that similar sophisticated machinery is used in our cells.

Ohsumi's discoveries led to a new paradigm in our understanding of how the cell recycles its content. His discoveries opened the path to understanding the fundamental importance of autophagy in many physiological processes, such as in the adaptation to starvation or response to infection. Mutations in autophagy genes can cause disease, and the autophagic process is involved in several conditions including cancer and neurological disease.

Source:
https://www.nobelprize.org/nobel_prizes/medicine/laureates/2016/press.html
https://en.wikipedia.org/wiki/Yoshinori_Ohsumi

CARTOON



"...and this is Ralph, your anesthesiologist."

MOLECULE OF THE MILLENIUM

Ac1903

In a recent study, new smaller molecule AC1903 was found to be very effective in preventing the advancement of progressive kidney diseases. Progressive kidney diseases are often associated with scarring of the kidney's filtration unit, a condition called focal segmental glomerulosclerosis (FSGS). This scarring is due to loss of podocytes, cells critical for glomerular filtration, and leads to proteinuria and kidney failure.

Inherited and sporadic forms of FSGS are caused by mutations in genes that encode regulators of the actin cytoskeleton—specifically, modulators of Rac1. Mutations in these genes, including ARHGAP24, ARHGDIA, and ARHGEF17, result in excess Rac1 signaling in podocytes. Activation of Rac1 signaling leads to the vesicular insertion of transient receptor potential canonical–5 (TRPC5) ion channels into the podocyte plasma membrane, making them available for activation by receptors such as the angiotensin II type 1 receptor (AT1R). This results in transient Ca_2^+ influx into the podocyte, and further Rac1 activation, feeding a circuit that promotes podocyte cytoskeletal remodeling. Study was on focused on this Rac1-TRPC5 pathway, to find whether this pathway is responsible for disease progression in FSGS and, if so, can it be blocked for therapeutic benefit?

Current therapy for FSGS consists of off-label use of nonspecific medications, which do not alter the progression of disease and are associated with toxicities. A small molecule, AC1903, that specifically blocks TRPC5 channel activity in glomeruli of proteinuric rats was identified in the study. Chronic administration of AC1903 suppressed severe proteinuria and prevented podocyte loss in a transgenic rat model of FSGS. AC1903 also provided therapeutic benefit in a rat model of hypertensive proteinuric kidney disease.

Animal data obtained in the study demonstrated that a specific TRPC5 small-molecule inhibitor administered at the time of severe, established proteinuria, but before creatinine is elevated, can rescue podocytes and attenuate the progression of morphologic and molecular changes that characterize FSGS. These findings provide a mechanistic rationale for therapeutically targeting TRPC5 channels, indicating that TRPC5 activity drives disease and that TRPC5 inhibitors may be valuable for the treatment of progressive kidney diseases.

Source: Anna Greka , Corey R. Hopkins, Yiming Zhou, Philip Castonguay. A small-molecule inhibitor of TRPC5 ion channels suppresses progressive kidney disease in animal models. Science 358, 1332–1336 (2017) DOI: 10.1126/science.aal4178

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REGULATORY CHANGES IN INDIA'S LANDSCAPE (2005–2017)

Clinical trials for any drug shall be initiated only after the permission granted by the regulatory authority and the respective ethics committee(s). Clinical trials must be conducted as per schedule Y and ICH-GCP guidelines. The Schedule Y amendment released on 20th January, 2005 saw dramatic changes that attempted to bring India on par with internationally prevalent regulations. Some of the key changes included the definition of a clinical trial, permitting trials in India to be conducted in the same phase of drug development as elsewhere in the world, demarcation of clear roles and responsibilities of the sponsor, investigator and ECs, underscoring the importance of informed consent, requirement for studies in special populations and mandating that protocol amendments need approval from the office of the DCGI. In the following table, we have extracted out few of the important amendments carried out during last ten years:-

G.S.R./notification number with year/date	Nature of the amendment/gazette notification/regulation
G.S.R. 32(E) dated 20th January, 2005, IInd amendment	Amendment 1988 version of Schedule Y. Key features - definition of clinical trial, and clear identification of responsibilities of sponsor, investigator, ECs and permitting clinical trials to be conducted in the same phase as elsewhere in the world.
SO 1468 (E) dated 6th October, 2005	Devices such as cardiac stents, heart valves, intravenous cannulas, catheters, orthopedic implants and internal prosthetic replacements specified as drugs.
ICMR guideline dated October, 2006	The second revision of the guideline that is valid until 2016.
G.S.R. 53(E) dated 30th January, 2013	Introduction of compensation for clinical trial related injury or death and Introduction of SAE analysis and timelines for reporting SAEs.
G.S.R. 63(E) dated 1st February, 2013	Specifies various requirements conditions for conduct of clinical Mats (for example IEC approval, registration with CTRI, submission of annual status report) and Introduction of clinical trial inspections, and actions in case of noncompliance.
G.S.R. 72(E) dated 8th February, 2013	Registration of ECs with DCGI made mandatory.
File No GCT/20/SC/ClinJ 2013 DCGI, dated 19th November, 2013	Introduction of AV recording of informed consent process of clinical trials.
File no 12-01/14-DC Pt 47 dated 3rd July, 2014	Cap on the number of trials that could be conducted by an Investigator to three only. (n=3)
File no 12-01/14-DC Pt 47, dated 3rd July, 2014	Clinical trial waiver for approval of new drugs already approved outside India specified under certain conditions - national emergency, extreme urgency, epidemic and orphan drugs and drugs indicated for diseases in which no therapy exists.
File no 12-01/14-DC Pt 47 dated 3rd July, 2014	Medical devices may not need Phase 1 studies. However, the process of their clinical trials approval should be similar to that of drugs or vaccines.
File no 12-01/14-DC Pt 47, dated 3rd July, 2014	When placebos are used, the trial design should be appropriate, efficient and ethical.
File no. ECR/Misc/ Indt EC/007/2013 dated 30th July, 2013	Independent ECs registered by CDSCO to oversee Bioavailability and Bioequivalence studies only.
G.S.R 889(E) dated 12th December, 2014 effective from June, 2015	Clarification regarding compensation and free medical management in case of trial related injury. Change in timelines for SAE reporting.
G.S.R 611(E) dated 31st July, 2015	Modification and relaxation of AV consenting norms - for vulnerable populations only and where a NCE or NME is being studied.
GSR 313(E) dated 16th March, 2016	A 'new' drug undergoing a clinical trial for investigator initiated studies (IIS) no longer needs approval from the DCGI Approval.
DGFT notification dated 4th August, 2016	Indian diagnostic laboratories and research centers can import/export biological material without the need for an import/export license. They only need to submit an undertaking about the safe transfer and disposal of the biological material to the Customs at the port of entry/exit.
Circular by CDSCO, dated 2nd August, 2016	The only three trials per investigator norm revoked.
File 12-01/14-Pt 47, dated 2nd August, 2016	The condition that trials could not be conducted at sites with less than 50 beds revoked.
Circular by CDSCO, dated 3rd August, 2016	No approval needed from DCGI for addition of new trial site or investigator. Only IEC permission is required.
Notice by CDSCO; dated 5th October, 2016 (CDSCO/IT/ 2015-[48])	'SUGAM' portal for online applications for clinical trials as part of efforts to increase the transparency, and efficiency of processing clinical trial applications.
File no 12-01/14-DC Pt 47/DRS dated 29th November, 2016	Accreditation of ECs with NABH-Quality Control of India made mandatory from 1st Jan, 2018.

IEC - Institutional Ethics Committee ; AV - Audio visual ; EC - Ethics Committee ; DCGI - Drugs Controller General of India ; DGFT - Directorate General of Foreign Trade ; NCE - New Chemical Entity ; NME - New Molecular Entity ; SAEs - Serious Adverse Events

NEW DRUG APPROVAL

Giapreza

The U.S. Food and Drug Administration approved Giapreza (angiotensin II) injection on 21st December 2017 for intravenous infusion to increase blood pressure in adults with septic or other distributive shock conditions.

In a clinical trial of 321 patients with shock and a critically low blood pressure, significantly more patients responded to treatment with Giapreza compared to those treated with placebo. Giapreza effectively increased blood pressure when added to conventional treatments used to raise blood pressure. Giapreza can cause dangerous blood clots with serious consequences (clots in arteries and veins, including deep venous thrombosis), so prophylactic treatment for blood clots should be used.

Source: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm537040.html

Ozenoxacin

The U.S. Food and Drug Administration approved Ozenoxacin on 12th November, 2017 for the treatment of impetigo due to *Staphylococcus aureus* or *Streptococcus pyogenes* in adult and pediatric patients having age of 2 months and older. Ozenoxacin is supplied as an ointment for topical administration. Apply a thin layer of Ozenoxacin topically to the affected area twice daily for five days. Affected area may be up to 100 cm^2 in adult and pediatric patients of 12 years of age and older or 2% of the total body surface area and not exceeding 100 cm^2 in pediatric patients less than 12 years of age.

Ozenoxacin is a quinolone antimicrobial. The mechanism of action involves the inhibition of bacterial DNA replication enzymes, DNA gyrase A and topoisomerase IV.

Source: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100241/xepi-ozenoxacin-

DRUGS IN CLINICAL TRIALS:

Talazoparib significantly extends Progression-Free Survival (PFS) in Phase 3 EMBRACA trial of patients with Metastatic Breast Cancer

Talazoparib is an investigational, oral, dual-mechanism poly ADP ribose polymerase (PARP) inhibitor that is taken once daily. Recently, Pfizer Inc. announced that the Phase 3 EMBRACA trial in patients with germline (inherited) BRCA1/2-positive (gBRCA+) locally advanced and/or metastatic breast cancer (MBC) demonstrated superior progression-free survival in patients treated with Talazoparib, compared to patients who received physician's choice standard of care chemotherapy. Median PFS was 8.6 months for patients treated with Talazoparib and 5.6 months for those treated with chemotherapy. This represents a 46% reduction in the risk of disease progression.

Source: http://press.pfizer.com/press-release/talazoparib-significantly-extends-progression-free-survival-phase-3-embraca-trial-pati

Erenumab Phase 3 STRIVE data published in The New England Journal of Medicine (NEJM) demonstrate significant, sustained efficacy in Migraine Prevention – Amgen announced that the NEJM published positive results from the six-month Phase 3 STRIVE study evaluating Erenumab versus placebo for the prevention of episodic migraine (between four and 14 migraine days per month). Patients taking Erenumab experienced a significant reduction in mean monthly migraine days and were significantly more likely to achieve a 50 percent or greater reduction in monthly migraine days than those taking placebo. Erenumab is the first and only fully human monoclonal antibody designed to specifically block the calcitonin gene-related peptide (CGRP) receptor; CGRP plays a critical role in migraine activation.

Source: https://www.prnewswire.com/news-releases/aimovig-erenumab-phase-3-strive-data-published-in-the-new-england-journal-of-medicine-demonstrate-significant-sustained-efficacy-in-migraine-prevention-300563824.html

DIETARY RESEARCH:

Low Folate, Vitamin D implicated in First-Episode Psychosis

Nutritional deficiencies, especially deficiencies in folate and vitamin D, are associated with first-episode psychosis (FEP), new research suggests. Australian researchers found significantly lower levels of folate and vitamin D in patients with FEP, compared to healthy control persons. Limited evidence also suggested that serum levels of vitamin C were reduced in people with FEP.

"The extent of nutritional deficiencies was present right from illness onset," said lead author Joseph Firth, PhD, NICM, School of Science and Health, University of Western Sydney, Australia.

Source: https://www.medscape.com/viewarticle/890499

NEW MOLECULE ENTITY & NEW THERAPEUTIC BIOLOGICAL PRODUCT:

Netarsudil

December 18, 2017 – The U.S. Food and Drug Administration approved RHOPRESSA® (Netarsudil ophthalmic solution), a Rho kinase inhibitor for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The recommended dosage is one drop in the affected eye(s) once daily in the evening.

Source: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=208254

Ertugliflozin

December 19, 2017 - The U.S. Food and Drug Administration approved STEGLATRO™ (Ertugliflozin), a a sodium glucose co-transporter 2 (SGLT2) inhibitor to improve glycemic control in adults with type 2 diabetes mellitus. Recommended starting dose is 5 mg once daily, taken in the morning, with or without food. Increase dose to 15 mg once daily in those tolerating STEGLATRO and needing additional glycemic control.

Source: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=209803

NOVEL USE OF MEDICATION:

Researchers at Cardiff University, in collaboration with the University of Dundee, have identified a drug molecule within a medicine used to treat tapeworm infections which could lead to new treatments for patients with Parkinson's disease.

Parkinson's disease is a long-term degenerative disorder of the central nervous system that, according to the Parkinson's UK, affects one person in every 500. That means an estimated 127,000 people are currently living with Parkinson's disease in the UK alone.

Over the last decade or so, researchers striving to find a cure for this debilitating disease have focused their attention on a protein found in the human body known as PINK1. It's understood that the malfunction of this protein is one of the leading causes of Parkinson's disease.

Several studies have suggested that discovering a drug which is capable of enhancing the function of PINK1 could be a significant step in halting neurodegeneration and therefore slow down or even treat Parkinson's disease.

With this knowledge in mind, researchers at Cardiff and Dundee Universities have discovered that a drug traditionally used to treat tapeworm infections, named **Niclosamide**, is also an effective activator of the PINK1 protein.

Furthermore, the research, funded by The Welcome Trust, revealed that Niclosamide and some of its derivatives could enhance PINK1 performance within cells and neurons. This has given the researchers reason to believe that this drug could provide new hope for patients living with Parkinson's disease.

Dr. Youcef Mehellou, from Cardiff University's School of Pharmacy and Pharmaceutical Sciences, who co-lead the study, said: "This work represents the first report of a clinically used drug to activate PINK1 and may hold promise in treating Parkinson's disease. We will now take our findings to the next level by evaluating the ability of Niclosamide to treat Parkinson's disease in disease models. This is an exciting stage of our research and we are positive about the long term impact it could have on patients' lives".

Source: https://www.europeanpharmaceuticalreview.com/news/70346/niclosamide-parkinsons-disease/
https://www.cardiff.ac.uk/news/view/1027540-tapeworm-drug-could-lead-the-fight-against-parkinsons-disease

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FACULTY ACHEIVEMENTS:

- Dr. R. Balaraman has been awarded Honorary Fellow of Indian Pharmacological Society (FIPS) on the occasion of Golden Jubilee Celebration by Western Regional Conference of Indian Pharmacological Society (WRIPSCON-2017) on 19th August, 2017 at Ahmedabad.
- Dr. Rajesh Maheshwari has been elected as the life Member of National Academy of Medical Sciences, India (MAMS) on 28th October, 2017 at Shri Guru Ram Das Institute of Medical Sciences, Amritsar during Convocation of National Academy of Medical Sciences (NAMSCON 2017).

DEPARTMENT OF PHARMACY ACTIVITIES

Pharmacy Week-2017:

Department of Pharmacy, SV celebrated Pharmacy Week from 20th - 23rd November, 2017. The celebration was a part of 56th National Pharmacy Week celebrations. The theme selected by Indian Pharmaceutical Association was "Know your Medicines: Ask your Pharmacist". On the first day, the program started with inauguration ceremony. Different competitions like Quiz, Elocution, Patient counseling, Poster, Essay writing as well as Health camp were organized on the consecutive days. The chief guest of the inauguration ceremony was Dr. Rajesh Bharaney, Hon. Vice Chancellor, SV and Guest of Honor was Dr. G. V. Shah, Dean, SBKS MI&RC. All students actively participated in the celebrations.

Children's Day- 2017:

On Tuesday, 14th November, 2017, Fourth Pharm. D students visited Government Balwadi in Piparia. BMI of the children were measured. The students along with faculty members of Department of Pharmacy then explained the proper healthcare regime to the school children. Students entertained the children by distributing chocolates and spread awareness about the ill effects of not taking proper nutrition that is required for the body.

World Diabetes Day- 2017:

Department of Pharmacy, SV celebrated 'World Diabetes Day' on Tuesday, 14th November, 2017. The theme proposed this year by the International Federation of Diabetes was 'Women and Diabetes - Our Right to a Healthy Future'. Aditya Mundra and Saurabh Mamtani, students of 5th Pharm. D delivered a brief talk on the theme.

World AIDS Day- 2017:

Department of Pharmacy, Sumandeep Vidyapeeth organized an Awareness Program on 'World AIDS Day" – 1st December 2017. Around 22 students from 4th and 5th year Pharm.D participated in the program. Students prepared informative leaflets & charts on AIDS which were distributed among the patients and their relatives who visited

LAUGH & LIVE LONGER

Patient: Oh Doctor, I am so nervous. This is my first operation.
Doctor: Calm down. This is my first operation, too.

Patient: Doctor, doctor, will I be able to play the violin after the operation?
Doctor: Yes, of course
Patient: Great! I never could before.

Book-Post

To, ...

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Department of Pharmacy
Sumandeep Vidyapeeth, Piparia, Vadodara (Gujarat)

Please email your suggestions, comments and contribution for next issue to editorpharmahorizon@gmail.com
Note: If you have any query regarding medication and disease please write us at: svdruginfo@gmail.com