

Bacteria Resistant Pacemaker

While the pacemaker or metal valve in heart does a fine job of protecting humans, it also runs the risk of infections due to the microbial films formed on its surface.

This is generally treated with a high dose of antibiotics. However, it does not help as the microbes become antibiotic resistant. In fact, the continuous release of antibiotics from the implants creates conditions for the growth of antibiotic-resistant strains of microbes.

Another disadvantage is the exhaustion of the antibiotic dose due to leaching. A study by a research group led by SampaSaha, professor, Department of Materials Science and Engineering, IIT Delhi, has proposed a non-leachable antimicrobial coating. The team created a biodegradable 3D-printed polymeric implant, which is modified with anti-infective polymer brushes.

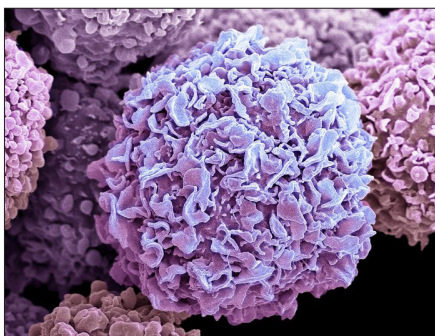
The implant itself is fabricated from a blend of bio-



degradable polyesters like polyester of tartaric acid, a natural acid found in tomatoes, grapes and raw mangoes; and polylactic acid from corn starch. Using the polyester as a scaffold, infection-resistant polymer brushes are chemically bonded to its surface. The nano-sized brushes, fabricated from poly[(2-methacryloyloxyethyl) trimethyl ammonium chloride], are antibacterial.

Breast cancer cells can evade immune attacks.

Scientists from the Indiana University (IU) Melvin and Bren Simon Comprehensive Cancer Center have discovered how breast cancer cells evade immune cells to survive. The findings could lead to more improved immunotherapy treatment for patients.



Xinna Zhang, Ph.D., and other collaborators observed that when breast cancer cells have higher concentrations of the protein, known as MAL2 on the surface of cells, the tumor cells can continue to grow by evading immune attacks. The study results were recently published in *The Journal of Clinical Investigation*.

Immunotherapy is regarded as the future of cancer treatment. It targets and kills cancer cells by harnessing the body's immune system. Interpreting how cancer cells evade immune attacks could provide new ways to enhance immunotherapy for patients, described Xiongbin Lu, Ph.D., Vera Bradley Foundation Professor of Breast

Cancer Innovation and cancer center researcher.

The study led the team to the MAL2 protein; it revealed that increased levels of the MAL2 protein in breast cancer, and particularly in triple-negative breast cancer (TNBC), was associated with poorer survival of patients.

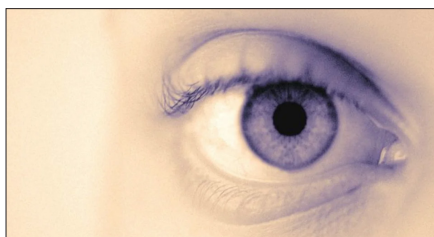
"Tumor cells can evade immune attacks; with less MAL2, the cancer cells can be recognized and killed by the immune system. MAL2 is a novel target. By identifying its function in cancer cells and cancer immunology, we now know its potential as a cancer immunology target," Lu concluded.

Eyes may signal risk for Stroke and Dementia

Eyes may be a window into the health of brain, a new study indicates.

Researchers found that older adults with the eye disease, retinopathy, were at increased risk of having a stroke, as well as possible symptoms of dementia. And on an average, they died sooner than people their age without the eye condition.

Retinopathy can lead to vision changes, such as trouble reading or seeing faraway objects. In the later stages, the damaged blood vessels may leak and cause visual disturbances like dark spots or cobweb-like streaks, according to the U.S.



National Eye Institute (NEI).

In the new study, researchers found that people with signs of retinopathy were twice as likely to report a history of stroke, versus those with no evidence of the eye disease. Similarly, they were 70% more likely to report memory problems, a potential indicator of dementia.

The results are based on more than 5,500 U.S. adults who took part in an ongoing government health study. All of them underwent retinal scans to look for retinopathy. On an average, people with retinopathy had heightened risks of stroke and memory issues, even after age, diabetes and high blood pressure were taken into account.

The findings support adding retinopathy to the list of factors doctors consider in gauging patients' stroke risk, according to Daniel Lackland, a volunteer expert with the American stroke association.

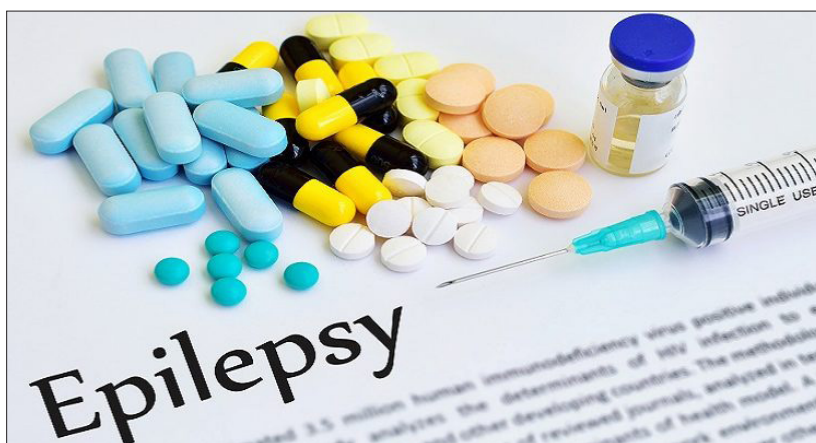
New Anti-epileptic Drug Brivasure

Alkem Laboratories Ltd, one of the India's leading pharmaceutical formulation development, manufacturing and marketing companies has announced the launch of Brivasure, an affordable anti-epileptic drug for the treatment of Epilepsy in India.

Brivasure, Alkem's anti-epileptic drug (AED) is a generic version of the parent molecule.

The drug has been approved by the Drugs Controller General of India (DCGI) in the adjunctive management of partial onset seizure with or without secondary generalization. The drug has exhibited faster onset of action, efficacy with favorable safety profile.

Dr. Akhilesh Sharma, President and Chief Medical Officer, Alkem, said, "The magnitude of epilepsy treatment gap in India is very high and ranges from 22% in urban to 90% in rural India. Making effective and high quality anti-epileptic drugs more affordable and accessible to these patients is the need of the hour. With the introduction of brivaracetam by Alkem, we are optimistic about making steady progress and



revolutionizing Epilepsy treatment in India as well as globally. Levetiracetam has been considered as a broad-spectrum antiepileptic drug in India but after the clinical usage for over a decade we have learnt that it has got its own disadvantages and is associated with certain behavioral side effects. Brivaracetam seems to be filling up this gap with its promising efficacy which was observed even in those patients who had previously discontinued Levetiracetam due to side effects, benign side effects and simpler dosing regimen making it more convenient and cost-effective proposition for the patients."

NSD3 is the main driver of Squamous Cell Carcinoma of the Lung

A chromatin-regulating enzyme has been shown to be a key driver of a common type of lung cancer. Drugs that target the enzyme could improve treatment and survival rates for this particular cancer.

“Squamous cell carcinoma represents nearly one third of all lung cancers in humans,” said KAUST structural biologist Lukasz Jaremko, who led the research along with colleagues at Stanford University and The University of Texas MD Anderson Cancer Center, U.S. “Our joint structural and dynamics investigations, including enzymatic activity studies, genetic analyzes, mouse model and human cell results, all point to the enzyme histone-lysine N-methyltransferase (NSD3) as a main driver of cancer,” he added.

As part of the investigations, Ph.D. student Vladlena Kharchenko, a member of Jaremko’s lab, used nuclear magnetic resonance spectroscopy to experimentally evaluate the structure and dynamics of both normal NSD3 and the hyperactive mutant implicated in driving lung squamous cell carcinoma.

The mutation did not appear to affect the static structure of the enzyme. However, using the dynamic nuclear Overhauser effect, scientists were able to



show that the hyperactive mutation led to mobility changes in part of the NSD3 enzyme, enabling it to more easily catalyze the addition of two methyl molecules to a histone tail in chromatin. This ultimately deregulates cancer-promoting genes in some forms of lung cancer.

“Our studies explain the molecular foundations of NSD3 enzymatic hyperactivity and unequivocally confirm that NSD3 is the main driver of squamous cell carcinoma of the lung,” said Jaremko.

Novel Pathogens may cause the Development of Colorectal Cancer

Scientists led by Harald zur Hausen, German virologist, detected the pathogens in colorectal cancer patients in close proximity to tumors. The researchers show that the BMMFs trigger local chronic inflammation, which can cause mutations via activated oxygen molecules and thus promote cancer development in the long term. BMMFs and inflammatory markers were significantly more frequently detectable in the vicinity of malignant intestinal tumors than in the intestinal tissue of tumor-free individuals.

A few years ago, scientists led by Ethel-Michele de Villiers at the German Cancer Research Center (DKFZ) discovered a novel form of infectious agents in dairy products and bovine sera. These were ring-



shaped DNA elements that showed great similarity to sequences of certain bacterial plasmids. They were named Bovine Meat and Milk Factors (BMMFs) after their origin in bovine products.

Scientists from Timo Bund’s team at the DKFZ have now carefully investigated this link using tissue samples from colorectal cancer

and from healthy intestine. To detect the pathogens, the researchers used antibodies generated against the Rep protein. This enabled them to detect BMMFs in 15 of 16 colorectal cancer tissue samples. Bund and colleagues looked for combined Rep/CD68 signaling in colorectal cancer samples and compared them with colorectal tissue samples from a group of younger cancer-free control subjects. In the cancer patients, 7.3 percent of all intestinal cells in the tumor environment were positive for combined Rep/CD68 signals. In the intestinal cells of the control group, this figure was significantly lower at only 1.7 percent.

“We therefore regard BMMFs as indirect carcinogens, which probably act on the dividing cells of the

intestinal mucosa for decades," zur Hausen said. He hypothesizes that infection with BMMFs usually occurs early in life, around the time of weaning. "The results support our hypothesis that the consumption of

milk and beef are causally linked to the development of colorectal cancer, and at the same time open up possibilities for preventive intervention," explains zur Hausen. For example, early detection of BMMFs

could identify individuals who are particularly at risk, who should then seek timely colorectal cancer screening.

The Role of SGLT-2 Inhibitors in Heart Failure

In addition to their glucose-lowering agents for treating type 2 diabetes mellitus (T2DM), the sodium-glucose cotransporter-2 (SGLT-2) inhibitors have demonstrated cardioprotective properties, making them particularly beneficial for management of patients with diabetes at risk of heart failure (HF), or those with HF.

The SGLT-2 inhibitors have been shown to significantly reduce atherosclerotic events, hospitalization for HF and cardiovascular and total mortality. Preferential use of SGLT-2 inhibitors is recommended for HF patients with T2DM, and data is emerging for HF patients without diabetes. Clinicians need to better integrate current guidelines and clinical data from

SGLT-2 inhibitor trials for preventing and treating HF patients with and without diabetes.

In addition, clinicians have gaps in their knowledge of newer therapies, including SGLT-2 inhibitors, and may not be familiar with recent evidence for their use in diabetic patients for the prevention and treatment of HF.



Low-Dose Aspirin may Immunize you from COVID-19

As the Israeli research team noted, aspirin is an anti-inflammatory drug and previous studies have shown that it may help the immune system combat some viral infections. According to the researchers, aspirin was widely used during the 1918 Spanish Influenza pandemic, several decades before its activity against RNA viruses was confirmed.

All of this prompted the team to investigate whether taking daily low-dose aspirin might reduce COVID-19 susceptibility, as well as the length of illness if infection does occur. The dose used in Israel was 75 milligrams (mg); low-dose aspirin in the United States is typically



a bit higher, at 81 mg.

The research was led by Eli Magen, from the Barzilai Medical Center in Ashkelon, Israel. His team tracked data on nearly 10,500 people who were tested for COVID-19 during the first wave of the pandemic in Israel, from February to the end of June of last year.

Among people who did get COVID-19, the time it took for SARS-CoV-2 PCR test results to go from positive to negative was significantly shorter among those who used aspirin, and the duration of their disease was two-three days shorter, depending upon preexisting health conditions.

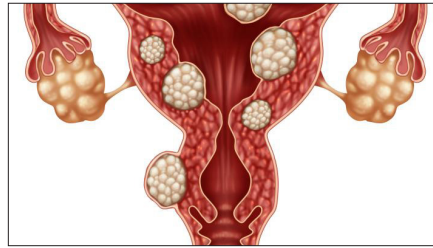
"This observation of the possible beneficial effect of low doses of

aspirin on COVID-19 infection is preliminary but seems very promising," said Magen. However, only larger studies, conducted in other hospitals and countries, can help confirm that aspirin had such a benefit, the researchers stressed.

Vitamin D and Egcg for the Management of Uterine Fibroids

Uterine fibroids are a widespread, significant health issue. Around 50% of women of reproductive age suffer from uterine fibroids. Sufferers face symptoms including abnormal uterine bleeding and pelvic pain that negatively affect quality of life. Yet, the existing pharmacological and surgical treatment options have downsides that mean many women forego treatment. A new, better treatment option is needed.

Around half of uterine fibroid cases are asymptomatic, although such people may have unrecognized symptoms including heavy uterine bleeding and fertility problems. In women who have symptoms, the condition manifests in a range of ways that are detrimental to their health and quality of life such as anemia and bladder pressure.



The severity of the symptoms leads some women to undergo hysterectomies to remove the fibroids. Development of additional surgical options including uterine artery embolization and radiofrequency thermal ablation enabled women to get relief from their fibroids without undergoing hysterectomies. However, those treatments still carry costs and complications, including potentially the persistence of the diminished fertility associated with uterine fibroids.

The body of research suggested vitamin D and EGCG may inde-

pendently have some positive effects on uterine fibroids through mechanisms such as the down-regulation of catechol-O-methyltransferase and inhibition of matrix metalloproteinase. However, there remained scope to improve on the effect either molecule achieved in isolation on key outcomes such as symptom improvement and volume reduction.

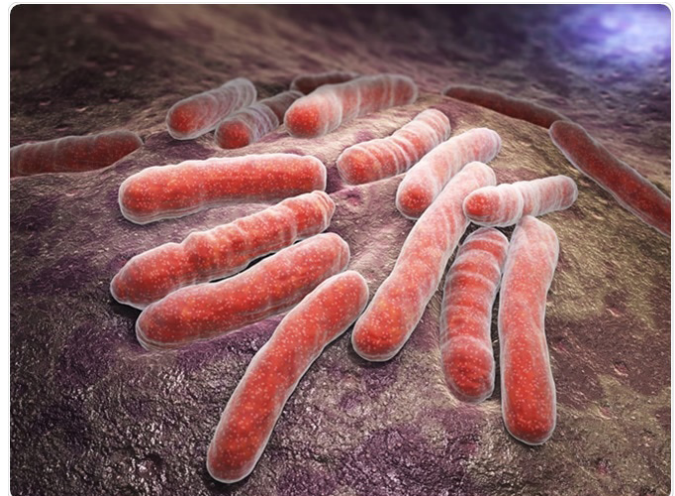
The clinical trial suggests Lo.Li.'s Delphys formulation of vitamin D and EGCG may address the need for treatments that bring symptomatic relief and reduce fibroid size without affecting fertility or causing other harms. Researchers are now building on those encouraging signs by gathering further evidence of the safety and efficacy of vitamin D and EGCG in the treatment of uterine fibroids.

Role of a Toxin-antitoxin System in TB

The tuberculosis bacterium is notorious because of its ability to stay dormant for years within the human body. Now, a study by researchers at Translational Health Science and Technology Institute (THSTI), Faridabad, and Institute of Microbial Technology (IMTech), Chandigarh, has investigated a novel molecular pathway that helps the bacteria to avoid being noticed by the immune system.

The team of researchers provide new insights into the role of VapBC22, a toxin-antitoxin system, in helping the bacteria to evade the host immune response and establish infection. Whether the bacteria remain dormant or establish infection in their host, the process is facilitated by a pair of linked genes called a toxin-antitoxin system. One of these genes produces a 'toxin' that can disrupt bacterial cell growth and function under unfavorable conditions, while the other produces an 'antitoxin' which can neutralize the toxin. At least 90 such toxin-antitoxin systems are known so far in the tuberculosis bacteria.

In the VapBC22 (Virulence-associated protein B and C22) system, VapC22 is the toxin and VapB22 is



the antitoxin. An earlier study indicated that VapB22 was essential for the growth of tuberculosis bacteria.

The study suggests that a relatively balanced expression of the VapBC22 toxin-antitoxin system is essential for the tuberculosis bacteria to adapt to the environment inside their host, and to sneakily proliferate without being spotted by the host immune system.

tem. This is necessary for the bacteria to subsequently establish a successful tuberculosis infection.

Based on their observations, the researchers view VapBC22 as an important drug target for tuberculosis treatment.

Type 2 Diabetes Leads to Increased Risk for Parkinson's Disease

New analyses of observational as well as genetic data have suggested that type 2 diabetes is tied to an increased risk for Parkinson's disease.

Two separate analyses were conducted, a meta-analysis of observational studies looking into the association between type 2 diabetes and Parkinson's and a Mendelian randomization analysis of genetic data on these two conditions. Similar results were obtained in both studies.

The observational data indicated that type 2 diabetes was associated with a 21% increased risk for Parkinson's disease while the genetic data pointed to an 8% increased risk. The findings also pointed that type 2 diabetes might be linked with faster progression of Parkinson's symptoms. The analyses were reported in a paper published in *Medscape*.



Treatment of Renal Fibrosis by Showing that it is caused by Telomere Shortening

The strategy of treating certain diseases by acting on the shortening of telomers is being pursued by the Telomeres and Telomerase Group of the Spanish National Cancer Research Centre (CNIO), which has already succeeded in curing pulmonary fibrosis and infarctions in mice by lengthening telomeres.

Recently they took first step towards doing the same with renal fibrosis by demonstrating that short telomeres are at the origin of this disease, which is also associated with aging. The new study is published in the journal *Nature Aging*.

"These results show the important role short telomeres play in its development, and this finding undoubtedly opens new doors for the treatment of renal fibrosis," said the first author of the study, Sarita Saraswati, a researcher with the Telomeres and Telomerase Group at CNIO.

The authors, headed by Maria A. Blasco, also offer a possible link between short telomeres and kidney fibrosis. Short telomeres exacerbate epithelial-to-mesenchymal transition (EMT) in the kidneys and thus promote pathological scarring of kidney tissue, i.e. fibrosis.

In this study, the researchers observed that telomere shortening alone is not enough to cause renal fibrosis, which is to be expected because the disease does not affect 100% of elderly persons. However, if mice with short telomeres were exposed to low doses of a kidney toxin, they did develop kidney fibrosis. "The mice reproduced all the symptoms of the human disease," explains Blasco.



As a final demonstration of the importance of telomeres in kidney fibrosis, the authors cultured kidney cells in which they expressed the gene for the telomerase enzyme, which elongates telomeres. In these cells with restored telomeres, the epithelial-to-mesenchymal transition program returned to normal, and the cells regained their healthy, pre-fibrosis appearance.

"As short telomeres accumulate with aging in the organism, it is tempting to speculate that pathological EMT programs associated with aging, such as cancer and different types of tissue fibrosis, may be originated at least in part by the presence of short telomeres," the authors conclude.

Benefits of Psychedelic Micro Dosing and the Placebo Effect

Taking micro doses of psychedelic drugs for their possible mental health benefits has been growing in popularity recently. However, research investigating the medical value of micro dosing has been inconclusive. Now, researchers at Imperial College London (ICL) in the United Kingdom have introduced a novel control mechanism into such investigations. The ICL researchers identified a strong placebo effect in the perceived benefits of psychedelic micro dosing.

The study was conducted online with 191 individuals who were already micro dosing psychedelics for their mental well-being. Researchers guided participants through a procedure where they mixed their psychedelics with identical-looking placebo capsules. The study authors referred to this arrangement as "self-blinding."

"On the one hand, we observed micro dosing's benefits in a wide range of psychological measures. On the other hand, we saw equal benefits among participants taking placebos." said the lead author Dr. Balázs



Szigeti. "These findings suggest that the benefits are not due to the drug, but rather due to the placebo-like expectation effects. Many participants who reported that they experienced positive effects while taking the placebo were shocked to learn after the study that they hadn't been taking the real drug," he added.

Energy Deficiency in Brain Cells may Increase Parkinson's Risk.

A team of researchers at the Indian Institute of Technology (IIT) Madras has found that energy deficiency in certain cells in the human brain is a major cause for Parkinson's disease, a neurodegenerative disorder.

According to the team, it is known that Parkinson's disease is caused by the loss of dopaminergic cells (located in the central nervous system) in substantia nigra pars compacta (SNc), a key component of the ventral midbrain.

"The sequence of the three computational studies suggests that metabolic deficiency within the



basal ganglia circuit is the common underlying factor at the subcellular, cellular and network level in Parkinson's disease. Thus, we have a reasonably comprehensive theory of the pathogenesis of Parkinson's disease," said V. Srinivasa Chakravarthy from the institution.

At the subcellular level, metabolic deficiency leads to changes like including alpha-synuclein aggregation, reactive oxygen species production, calcium elevation, and dopamine dysfunction, which are characteristic subcellular changes in Parkinson's disease, the study indicated. This research aims to build a simplified model of the whole brain and use it to develop applications in medicine and engineering, the team said.

Parkinson's disease is the second most prominent neurodegenerative disease around the globe after Alzheimer's disease.

Combination of 3 Drugs for Advanced Breast Cancer

A combination of three drugs is safe and shows signs of effectiveness in treating some patients with previously treated advanced breast cancer, shows a clinical trial. The 'triplet therapy' combines the hormone therapy fulvestrant with two targeted drugs, called palbociclib and taselesib, that block cells from

multiplying and dividing.

A total of 78 patients with breast or other cancers were enrolled in the trial, and were given either the triplet therapy or a 'doublet' therapy of the targeted drugs without fulvestrant. The triplet therapy showed particular promise in the 25 patients with advanced

and previously treated estrogen receptor positive, HER-2 negative breast cancer with mutations in the PIK3CA gene, with more than one third of patients with this type responding. Mutations in the PIK3CA gene are the most common mutation in this type of breast cancer.

The trial was led by a team at The Institute of Cancer Research, London, and The Royal Marsden Hospital NHS Foundation Trust.

Professor Nicholas Turner, Professor of Medical Oncology at the ICR and Clinical Medical Oncologist at the Royal Marden Hospital NHS Foundation Trust, said, "The combination of retroviral drugs transformed HIV treatment and the combination of drug therapies now presents an exciting frontier in cancer research. Combining new and existing therapies is key to developing more treatments with more durable response. By using combinations that aims to treat cancer in multiple different ways, we hope we can stop cancer from developing resistance early on. Our study shows that a combination of drugs targeting a common breast

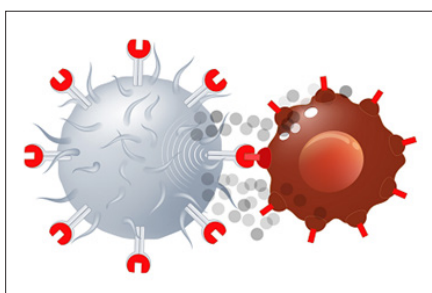


cancer mutation is a safe treatment option and already seems effective for some patients. This study was an important proof of concept for combining CDK4/6 and PI3K inhibitors and has enabled further studies with these drug types to move forward."

CAR T-Cell Therapy Approved for by FDA for indolent FL.

The Food and Drug Administration (FDA), USA, has granted accelerated approval to Yescarta (axicabtageneiciloleucel; Kite Pharma) for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after 2 or more lines of systemic therapy.

Yescarta carries a Boxed Warning regarding CRS and neurologic toxicities. Due to these potentially life-threatening reactions, the treatment is only available through a restrict-



ed program called the Yescarta and Tecartus REMS program.

Yescarta is also indicated for the treatment of adults with relapsed or refractory large B-cell

lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

The product is available as a cell suspension for infusion containing 2×10^6 CAR-positive viable T cells per kg of body weight, with a maximum of 2×10^8 .

Placenta: A Dumping Ground for Genetic Defects?

In the first study of the genomic architecture of the human placenta, scientists at the Wellcome Sanger Institute, the University of Cambridge and their collaborators have confirmed that the normal structure of the placenta is different from any other human organ and resembles that of a tumor, harboring many of the same genetic mutations found in childhood cancers.

The study, published in *Nature*, found evidence to support the theory of the placenta as a 'dumping ground' for genetic defects, whereas the fetus corrects or avoids these errors. The findings provide a clear



rationale for studying the association between genetic aberrations and birth outcomes, in order to better understand problems such as premature birth and still-birth.

It has long been known that the placenta is different from other human organs. In 1-2% of pregnancies, some placental cells have a different number of chromosomes to cells in the fetus, a genetic flaw that could be fatal to the fetus, but with which the placenta often functions reasonably normally.

Despite this genetic robustness, problems with the placenta are a major cause of harm to the mother and unborn child, such as growth restriction or even still-births. The team discovered that each one of these biopsies was a genetically distinct 'clonal expansion' - a cell population descended from a single common ancestor, indicating a clear parallel between the formation of the human placenta and the development of a

cancer.

Analysis also identified specific patterns of mutation that are commonly found in childhood cancers, such as neuroblastoma and rhabdomyosarcoma, with an even higher number of these mutations in the placenta than in the cancers themselves. Professor Steve Charnock-Jones, a senior author of the study from the University of Cambridge, said: "Our study confirms for the first time that the placenta is organized differently to every other human organ, and in fact resembles a patchwork of tumors. The rates and patterns of genetic mutations were also incredibly high compared to other healthy human tissues."

Now that the link between genetic aberrations in the placenta and birth outcomes has been established, further studies using larger sample sizes could help to uncover the causes of complications and diseases that arise during pregnancy.

Clinical Efficacy of the Accompanying Flavor in a Cold and Cough Syrup

Medications available over-the-counter (OTC) for the treatment of cold and cough are not only effective in giving the symptomatic relief but are also pleasant to take so as to encourage compliance.

A new syrup formulation for the symptomatic relief of cold, chills, and productive cough was developed containing paracetamol, guaifenesin and phenylephrine hydrochloride. These are active ingredients and well-established pharmaceutical agents and as a combination they deliver relief from several concurrent symptoms of colds and flu, i.e., sore throat, cough, headache, body ache, fever and nasal congestion. A flavoring agent known as flavor 316282, is added with these ingredients that causes a warm sensation in the mouth and back of the throat to soothe patients with cold and cough.

The main objective of the study published in *SAGE Open Med* was to evaluate the warming sensation that was produced by flavor 316282 in a cold and cough product. The study recorded the onset and disappearance of any warming sensation in the mouth or throat



of the participants. Participant's assessment of the sensation, taste, texture, and tolerability of the product as a cold and cough remedy was examined by using questionnaires.

Thus, the study concluded that flavor 316282 in cold and cough syrup is related to a warming sensation and is well tolerated, safe, and also palatable.