Department of Pharmacy

BRAC UNIVERSITY
Inspiring Excellence

PHARMA HIGHLIGHTS

ISSUE 51 | DECEMBER 2018

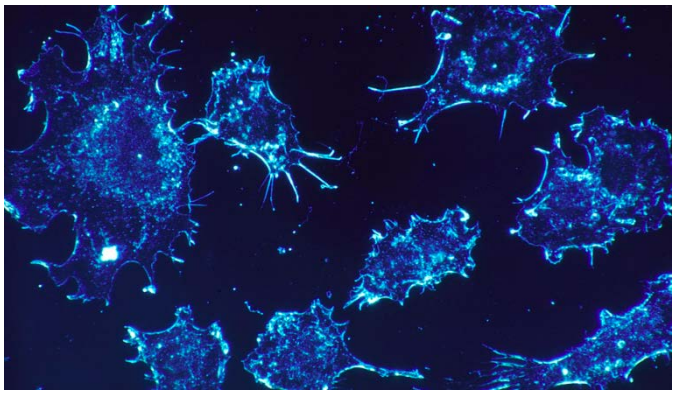
A Bacterial Protein Can Encourage Cancer Development

Researchers have discovered that a protein called DnaK made by the bacterium mycoplasma has the potential to disrupt the ability of cells infected with mycoplasma. As a result, the cell cannot repair their DNA damage. This unrepaired genetic damage can lead to cancer.

Researchers mentioned infection as a cause of approximately 20 percent of cancers. Most are known to be due to viruses. Their work provides an explanation for the mechanism of how a bacterial infection can trigger a series of events that lead to cancer. Of specific importance, the protein did not need to be continuously present in all cancer cells to be detrimental. The rate of lymphoma development was observed in groups of immuno-compromised mice that had been either infected with a strain of mycoplasma obtained from an HIV patient, or not. The infected mice got lymphoma at a younger age than the uninfected mice. Only some of the mouse cancer cells were found to carry bacterial DNA.

The scientists observed some bacterial proteins in cells infected by mycoplasma, which can disrupt a cell's natural anticancer proteins. However, DnaK reduces the activity of important cellular proteins involved in DNA repair and anticancer activities, such as p53. Thus, cells infected with mycoplasma would not be able to properly repair damaged DNA, potentially increasing the risk of cancer development. The researchers also noted that when cells are infected by bacteria, they release DnaK, which also entered nearby uninfected cells.

The amino acid sequences of DnaK were analyzed from many bacteria and it was found that the DnaK proteins from bacteria associated with cancer were different from bacteria that are not associated with cancer.



Source: AAAS/Eurekalert! Via UMSOM, PNAS

FDA Approves Two New Drugs for Cancers With Specific Genetic Mutations

Recently, FDA approved two new drugs and both of them target cancers with specific genetic mutations. Among the two drugs, first one Vitrakvi (larotrectinib), belongs to a new class of cancer drugs that are called “Tissue Agnostic” that treats cancer with particular genetic mutations. The difference between two drugs are the use of biomarker. The first drug is used to treat cancers based on a common biomarker across different types of cancers rather than the location of the tumor in the body, it is the second drug of this type to be approved by the FDA.

Vitrakvi is used for patients having solid tumors and must be metastatic which have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without acquired resistance mutation. NTRK is a gene family that encodes tropomyosin receptor kinases (Trk) which can be fused to other genes abnormally leading to increased growth signals that lead to cancer.

The FDA approved Vitrakvi based on three clinical trials of 55 pediatric and adult patients that showed 75% overall response rate lasting from 6 months to one year.

The second drug Xospata (gilteritinib) is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with FLT3 mutation. Xospata targets this gene and is the first drug to be approved that can be used alone in treating patients with AML having FLT3 mutation who have relapsed or who do not respond to initial treatment.

Xospata was approved based on a clinical trial of 138 patients with relapsed or refractory AML with FLT3 mutation, 21% of patients showed complete remission.

FDA recently also approved another drug Daurismo (glasdegib) for AML patients who are 75 years of age or older or who have chronic diseases.

Source: FDA

Department of Pharmacy

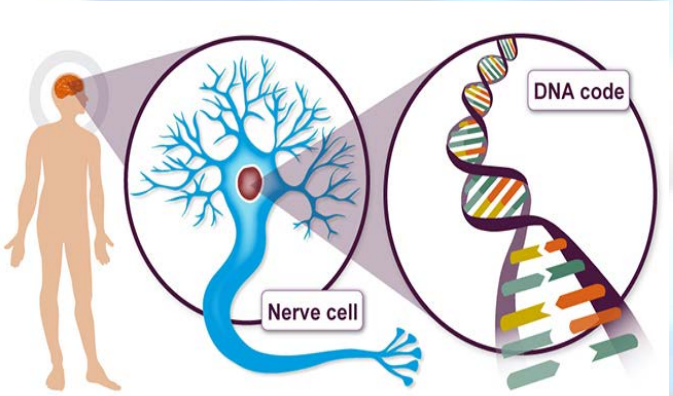
BRAC UNIVERSITY
Inspiring Excellence

PHARMA HIGHLIGHTS

ISSUE 51 | DECEMBER 2018

Alzheimer Preventing Drug Could Work Like a Vaccine

Apolipoprotein E (ApoE) is a protein found predominantly in the brain, which is responsible for carrying lipids and cholesterol around the brain and plays an important role in various repair mechanisms. Essentially, a particular subtype, ApoE4, works by promoting the accumulation of the b-amyloid protein that causes plaques seen in the brains of Alzheimer patients. Later, it was found that individuals who carry ApoE4 are up to 10 times more likely to develop Alzheimer's than those with other Apo subtypes. Researchers at UT Southwestern believe that ApoE4 is a primary factor in late-onset Alzheimer's disease. This inspired the development of a potential 'vaccine' drug that may be administered before age 40 for the potential prevention of the disease in about 50 to 80 percent of at-risk adults.



The ApoE4 protein not only increases plaque formation in the brain but has been confirmed to suppress and trap synaptic receptors within intracellular vesicles. Researchers believe that reversing the effects of ApoE4 via pharmacological and genetic inhibition of a certain protein, NHE6, which is involved in the acidity of endosomal vesicles, will likely prevent the late-onset of Alzheimer's disease. This novel therapeutic approach was further shown to be been successful in mice.

"If we can negate the ApoE4 process early, we may be able to prevent late-onset Alzheimer's altogether for many people so that they will never get sick," explained Dr. Joachim Herz, UT Southwestern molecular biologist and Alzheimer's expert.

While most Alzheimer's research has focused on halting the formation of amyloid and tau protein aggregates once they exist in the brain and degeneration has already begun, this study aimed to stop the overall degeneration process earlier, before the formation of the aggregates

The next step in this research is to develop small molecule inhibitors that can enter the brain efficiently and selectively block NHE6.

Source: UT Southwestern Medical Center

Autism Risk Increased by Mutations in Non-Coding Regions

In recent years, there has been some progress on learning the potential causes of autism. A work reported in Science described that new genetic mutations in the human genome, in non-coding regions called promoters, could play a role in the development of autism.

The research utilized and assessed genetic data from 2,000 families called quartets-two parents and two children, one child with autism and one without, from the Simons Simplex Collection of genetic data. Hence, the study gathered a large enough amount of data to find a significant role for mutation in promoter regions. The scientists discovered that children with autism have more spontaneous and uninherited mutations (de novo mutations) in the promoter regions compared to their siblings without autism. Some mutations that occurred in promoters were upstream of genes that interact with a common autism risk gene called CHD8, or other genes involved in development or neurodifferentiation.

Scientists also revealed that the eventual long-term payoff of the study may be in pointing to particular places and times in brain development that you want to focus on, from the many possibilities.

As such, proposed future studies focused on another massive collection of genetic data to advance this work even further. The SPARK cohort involves around 21,000 families, with more enrollment planned.

"SPARK is the largest study of autism in the United States," said lead investigator Wendy Chung of Columbia University. "With a goal of studying over 50,000 individuals with autism, we will be confident of the genetic factors we identify.

Source: AAAS/Eurekalert! via Simons Foundation, Science