DNA Repair - Autophagy

Carefully considered, the following information will provide details that can be verified by interested parties for how coronary plaque can be formed.

In 2016 the Nobel Prize was awarded for autophagy.

The following Chargaff maxim applies to that cellular mechanism for DNA repair.

"Science is wonderfully equipped to answer the question '**How**?' but it gets terribly confused when you ask the question '**Why**?' "
Erwin Chargaff; a member of the Watson and Crick DNA team (1905 – 2002)

Research has identified the fact that autophagy exists and many outcomes that the mechanisms performs to repair DNA. With that said, explicit and verifiable explanations for **How** the mechanisms function have not been fully elucidated.

The following information is provided as a basis from which additional details for the mechanism can be provided as part of discussions for the spectrum of DNA repair mechanisms that include autophagy.

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Based on DNA repair modeling we have been able to explain the role of CXCL5 and its interaction with CXCL4 and 6 to comprise the enzymes that perform autophagy on carbohydrates.

With that said, DNA repair requires homeostasis. The trefoil of CXCL1 - 3 have the amino acid constituents of histidine - arginine and lysine. They have a mutualistic relationship function to perform autophagy on

lipids. If imbalanced, the ability of CXCL4 - 6 will be disrupted and CV plaque can aggregated due to disruption homeostasis of the DNA repair mechanism of autophagy.

Note: To avoid confusion from excessive complexity, we have set aside discussions for the family of enzymes required to homeostasis of intracellular autophagy based on lysosomes. In other words, disruption of CXCL 4 - 6 for lipids can be the result of CXCL1 - 3 activities. How the disruption occurs can be explained to interested parties for independent verification after they have an understanding of DNA repair and copy error mutation mechanism.

https://medicalxpress.com/news/2017-11-protein-people-coronary-artery-disease.html

Could this protein protect people against coronary artery disease?

November 17, 2017 by Mark Derewicz

The buildup of plaque in the heart's arteries is an unfortunate part of aging. But by studying the genetic makeup of people who maintain clear arteries into old age, researchers led by UNC's Jonathan Schisler, PhD, have identified a possible genetic basis for coronary artery disease (CAD), as well as potential new opportunities to prevent it.

According to research published in the *American Journal of Pathology*, the protein CXCL5 is found in much higher levels in older adults with much clearer heart arteries. "CXCL5 looks to be protective against CAD, and the more CXCL5 you have, the healthier your coronary arteries are," said Schisler, assistant professor of pharmacology and member of the UNC McAllister Heart Institute. "Our findings suggest that there may be a genetic basis to CAD and that CXCL5 may be of therapeutic interest to combat the disease."

Schisler and his colleagues analyzed blood samples and heart scans from 143 people over age 65 who were referred to the UNC Medical Center in Chapel Hill for cardiovascular screening. The analysis revealed that people with clear arteries had markedly higher levels of CXCL5, as well as genetic variants near the CXCL5 gene, compared with people with more plaque.

CAD is the most common cause of heart attacks and the leading cause of death in the United States. Despite increased awareness of its risk factors and a variety of available treatment options, CAD has remained a persistent public health challenge.
Previous studies linked CXCL5 to inflammation, leading some researchers to assume the protein was harmful. But recent research in mice suggested the protein could help limit plaque buildup by changing the composition of fat and cholesterol deposits in the arteries. Schisler's finding offers the first evidence that CXCL5 could play a protective role in people, at least in the context of CAD.

In addition to offering clues about how CAD develops, the study opens new possibilities for prevention and treatment. For example, it may be possible to develop a drug that mimics the effects of CXCL5 or that increases the body's natural CXCL5 production to help prevent CAD in people at high risk. The protein could even potentially be leveraged to develop a new, nonsurgical approach to help clear clogged arteries.
"Another potential application of our findings is in the use of CXCL5 as a biomarker for CAD," Schisler said. "Although our goal was not to discover biomarkers that may have diagnostic or prognostic applications, it's possible and worth exploring."

One limitation of the study is that because all participants were referred for a heart scan, researchers did not include healthy patients. Further research is needed to confirm the role of CXCL5 in CAD and explore drug development opportunities.

Schisler said that for him, although the research is in its early stages, homing in on CXCL5 provides him and his team hope in a battle worth fighting.

"I lost both of my grandfathers to cardiovascular disease - one so early I do not even have any memories of him," he said. "This has been a driving force for me to not only understand heart disease, but also find treatments that allow people to live healthy, longer lives."

Explore further: **New clues in the quest to prevent clogged arteries**
More information: Saranya Ravi et al. Clinical Evidence Supports a Protective Role for CXCL5 in Coronary Artery Disease, *The American Journal of Pathology* (2017). **DOI: 10.1016/j.ajpath.2017.08.006**

Journal reference: American Journal of Pathology

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When we modeled CXCL5, the results indicated it was a zinc finger and copper-dependent protein kinase with isoleucine as the amino acid. This configuration matched our modeling of the form of vitamin B7 that we had identified as being one of the enzymes for autophagy.

In addition to CKCL5; Rac1 and Protein Kinase B (PKB) can also be verified as alternative designations for this cytokine.

The noteworthy part of this article and our findings are the correlations between obesity and type 2 diabetes. Obviously, when this research was done in 2009, knowledge of autophagy and “DNA” repair did not exist to the extent it does today.

This work further supports our hypothesis that different signaling molecules are responsible for obesity and T2 diabetes.

Molecule Discovered That Makes Obese People Develop Diabetes

ScienceDaily (Nov. 24, 2009) — Many people who are overweight or obese develop insulin resistance and type 2 diabetes at some stage in their lives. A European research team has now discovered that obese people have large amounts of the molecule CXCL5, produced by certain cells in fatty tissue.

The main risk factors for type 2 diabetes are obesity and a sedentary lifestyle. The biomedical community has known for many years that substances produced by fatty tissue are responsible for the link between obesity and diabetes. "Chronic inflammation of the adipose tissue, which is characteristic of obese people, is a crucial stage in the development of insulin resistence and type 2 diabetes," Lluis Fajas, lead author of the study and a researcher at the Institute of Health and Medical Research (Inserm) in France, said.

The results of this new study show that serum levels of a chemokine molecule called CXCL5, produced by certain adipose tissue cells, appear at much high levels in the tissues of obese people than in those of individuals with normal weight. This has helped Lluis Fajas's research team to come to a biomedically relevant conclusion: "The CXCL5 molecule helps cause insulin resistance and type 2 diabetes".

The most important part of this study, published in the journal *Cell Metabolism*, is the discovery that an experimental treatment aimed at inhibiting the action of CXCL5 can help to protect obese mice from developing type 2 diabetes. "If these studies can be confirmed in humans, this treatment would represent a fundamental improvement in the quality of life of obese individuals," the researcher concludes.

Bad habits cause obesity and diabetes

According to the latest data from the Spanish Diabetes Federation (FED), almost 3.5 million people in Spain have diabetes. This illness is most common in Andalusia and Murcia, regions where the highest percentage of people who are obese and sedentary. The specialists agree on the importance of prevention. Avoiding obesity, doing daily physical exercise and giving up smoking are some of the measures that could help to cut the number of diabetes cases by a half.

The International Diabetes Federation (IDF) says that more than 190 million people worldwide currently have diabetes. This figure will rise to 330 million by 2025, due to population growth, the ageing of the population, and increasing urbanisation and sedentary lifestyles. Obesity is the main avoidable risk factor in developing type 2 diabetes. Worldwide, 1.7 billion people are already at high risk of developing a non-contagious, weight-related illness, such as type 2 diabetes.

Obesity can reduce the life expectancy of people with type 2 diabetes by up to eight years, and 80% of people diagnosed with the illness are overweight at the time they are diagnosed.

At least half of all cases of type 2 diabetes among adults could be avoided if they did not put on weight. Taking action on lifestyle, such as changing diet and taking moderate physical exercise, can reduce the risk of developing type 2 diabetes by up to 60%.

| More

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Journal Reference:

1. Chavey et al. **CXC Ligand 5 Is an Adipose-Tissue Derived Factor that Links Obesity to Insulin Resistance**. *Cell Metabolism*, 2009; 9 (4): 339 DOI: 10.1016/j.cmet.2009.03.002

http://www.sciencedaily.com/releases/2009/11/091124103617.htm