**2- Mehdi Ghassan**

**Title: Metformin as a geroprotector drug**

**Abstract**

 Geroprotectors are [senotherapeutic](https://en.wikipedia.org/wiki/Senotherapeutics) agents and strategies that specifically target cellular senescence, an altered cell state associated with ageing and age-related diseases; in other word, geroprotectors aim to affect the root cause of aging and age-related diseases, and thus prolong the [life span](https://en.wikipedia.org/wiki/Life_expectancy) of animals. Some possible geroprotectors include [melatonin](https://en.wikipedia.org/wiki/Melatonin), metformin, and [carnosine](https://en.wikipedia.org/wiki/Carnosine).

Concerning metformin, apart from being a safe, effective and globally affordable glucose-lowering agent for the treatment of diabetes, such drug has earned much credit in recent years as a potential anti-aging formula. It has been shown that metformin significantly increase lifespan and delay the onset of age-associated decline in several experimental models. The current review summarizes advances in clinical research on the potential role of metformin in the field of geroprotection, highlighting findings from pre-clinical studies on known and putative mechanisms behind its beneficial properties. A growing body of evidence from clinical trials demonstrates that metformin can effectively reduce the risk of many age-related diseases and conditions, including cardiometabolic disorders, neurodegeneration, cancer, chronic inflammation, and frailty.  Moreover, due to the ability of metformin to induce autophagy by activation of 5' adenosine monophosphate-activated protein kinase, it is regarded as a potential hormesis-inducing agent with health-span-promoting and pro-longevity properties. Long-term intake of metformin is associated with low risk of adverse events; however, well-designed clinical trials are still warranted to enable potential use of this therapeutic agent as a geroprotector.

**3- Mustafa Hasan Fayroze**

**Title: Current and emerging treatments for hypercholesterolemia: A focus on statins and proprotein convertase subtilisin/kexin Type 9 inhibitors for perioperative clinicians.**

**Abstract**

The roles played by cholesterol in cancer development and the potential of therapeutically targeting cholesterol homeostasis are a controversial area in the cancer community. Several epidemiologic studies report an association between cancer and serum cholesterol levels or statin use, while others suggest that there is not one. Furthermore, the Cancer Genome Atlas (TCGA) project using next-generation sequencing has profiled the mutational status and expression levels of all the genes in diverse cancers, including those involved in cholesterol metabolism, providing correlative support for a role of the cholesterol pathway in cancer development. Cardiovascular disease is the major cause of death globally, with hypercholesterolemia being an important risk factor. The PCSK9 represents an attractive therapeutic target for hyper-cholesterolemia treatment and is currently in the spotlight of the scientific community. After autocatalytic activation in the hepatocyte endoplasmic reticulum, this convertase binds to the LDLR and channels it to the degradation pathway. This review gives an overview on the latest developments in the inhibition of PCSK9, including disruption of the protein-protein interaction (PPI) between PCSK9 and LDLR by peptidomimetics, adnectins and monoclonal antibodies and the suppression of PCSK9 expression by small molecules, siRNA and genome editing techniques. In addition, we discuss alternative approaches, such as anti-PCSK9 active vaccination and heparin mimetics.