Alpha1 MZ Foundation - Information & Research

News & Research Update

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Dear Subscribers,

As we know, most Alpha1 MZ patients have a fatty liver, and various medical names are used for them, which are also changing over time. I personally like NAFL (Non-Alcoholic Fatty Liver) the best because our fatty liver is not related to using alcohol. Maybe we should invent a new name, like the "A1AT-FL", because the Z mutation of the Alpha1 Antitrypsin is the leading cause of our fatty liver. Anyhow, we thought it was a good idea to expand a little bit on this subject.

Let's first discuss the leading cause of our Fatty Liver;

As you may already know, the Alpha1 Antitrypsin protein is produced in the liver, and the Mutated AAT "Z" protein is not correctly folded and can not get out of the liver cell. (The Endoplasmic Reticulum of the Hepatocyte). So, it gets stuck, polymerizes, and causes an inflammation process in the liver cells.
This "cleaning up" process is called Autophagy, and the speed of autophagy, which depends on other genes, determines the amount of liver damage. This explains why some Alpha1 "Z" patients get liver issues and others do not. We explained this in our previous newsletters with the 2024 scientific paper as a reference.

You also need to know that ER stress is a well-known cause of a fatty liver, as the paper from 2022 below explains.

Endoplasmic Reticulum Stress in Liver Diseases
The endoplasmic reticulum (ER) is an intracellular organelle that fosters the correct folding of linear polypeptides and proteins, a process tightly governed by the ER-resident enzymes and chaperones. Failure to shape the proper 3-dimensional architecture of proteins culminates in the accumulation of misfolded or unfolded proteins within the ER, disturbs ER homeostasis, and leads to canonically defined ER stress. In response to ER stress, the unfolded protein response (UPR) is activated to reestablish ER homeostasis ("adaptive UPR") or, conversely, to provoke cell death when ER stress is overwhelmed and sustained ("maladaptive UPR"). **It is well documented that ER stress contributes to the onset and progression of multiple hepatic pathologies, including non-alcoholic fatty liver disease (NAFLD)**, alcoholic liver disease (ALD), viral hepatitis, liver ischemia, drug toxicity, and liver cancers.

So now you know what the leading cause of your fatty liver is….

However, we cannot plead "not guilty" ourselves! Lifestyle and processed food intake changes started in the '60s, driven by commercial companies like Coca-Cola and McDonald's, also contribute significantly to our fatty liver.
This means that changing your lifestyle, eating healthy (non-processed) food, consuming less sugar and fat, etc., will greatly benefit your liver.

You should also be aware that our liver has no infinite capacity and that this capacity is reducing over time. So you may be an MZ and think, well… I have no liver issues. Be aware that at a certain point in your life, when you are getting older, the capacity of your liver will not be sufficient anymore. At that point, it is too late, and the deterioration will accelerate because your liver's regeneration capacity will

also be impaired. We have seen Alpha1 MZ patients going from Fatty Liver to stage 4 cirrhosis in about 2 years.

Bottom line: The leading cause of our Fatty Liver is the ER stress caused by the polymerization of the misfolded “Z” protein in the ER, further amplified by the Western lifestyle driven by the commercial interests of the food industry. And as I mentioned before, try to avoid foods with high-fructose corn syrup. It is just as bad for your liver as alcohol!

Here is a lovely well done short video explanation about high fructose corn syrup from the Cleveland Clinic: https://www.youtube.com/watch?v=MOOfdvdgxME

And, like always, enjoy the ride !!

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