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NEWS

Aging and COVID: similar pathways and the approach to cure

Edward Musinski[1]*, Gregory M. Fahy[2]

[1]Rating, Telewellness Ltd, London NW1 8UA, United Kingdom. [2]Medical College of Georgia, Augusta GA 30912, United States.

*Corresponding to: Edward Musinski. Rating, Telewellness Ltd, 52 Fitzroy Road, 322 Jacqueline House, London NW1 8UA, United Kingdom. E-mail: 1@lifetimeaward.live.

Coronavirus disease (COVID) 2019 is a disease of the immune system aging

Longevity experts have solutions. An integrative approach to both COVID and aging consequences mitigation was demonstrated at the ILA-Healthy Life Extension Society Conference. The report by Gregory Fahy on this topic was based on the paper "Reversing immunosenescence for prevention of COVID-19" [1].

Age is the strongest predictor of the severity and lethality of COVID-19 [2]. The reason of susceptibility to COVID-19 increase by age is an age-related decline of immune competence, or immunosenescence, the involution of the thymus by age [2].

Gregory Fahy has made first demonstrations of thymus regeneration inspired by the T cell. It is possible to both regenerate the thymus and reverse age-related immunological changes. The proposed Thymus Regeneration, Immunorestoration, and Insulin Mitigation Extension Trial protocol addresses the reversal of both epigenetic aging and immunosenescence, using a combination of drugs available in pharmacies [3]. T cell thymus regeneration is long-lasting in this case. In the case of SARS-CoV-1 infection, which is closely related to COVID-19, CD8 T cells have been shown to be able to persist 11 years post-infection [4].

Thymic involution in elderly people brings with it reduced production of thymic hormones such as thymosin alpha-1. Thymosin alpha 1 reduces the mortality of severe coronavirus disease 2019 by Restoration of Lymphocytopenia and Reversion of Exhausted T Cells [5].

The researchers at Spanish National Cancer Research Centre published a new work that suggests there is a link between shorter telomere lengths and the severity of COVID-19. What is the most important finding is that "the telomeres of the most seriously ill patients were also shorter, irrespective of age. It caught our attention that a common outcome of SARS-CoV-2 infection seems to be induction of fibrosis-like phenotypes in the lung and kidney, suggesting that the viral infection maybe exhausting the regenerative potential of tissues." [6]

In this work one also can find that the women on average had longer telomere lengths compared to the men, accounting for age. It is the reason why men might be harder hit with COVID-19.

Repurposed drugs

The existing repurposed drugs show great effects in both longevity and COVID-19 cases. For instance, mitogen-activated protein kinase kinase inhibitor trametinib, the mTOR complex 1 inhibitor rapamycin, and the glycogen synthase kinase 3 inhibitor lithium acts additively to increase longevity!

This triple drug combination increased lifespan by 48%. Furthermore, the combination of lithium with rapamycin cancelled the latter's effects on lipid metabolism. In conclusion, a combined approach, drug inhibitors of specific nodes may be the most effective way to target the nutrient-sensing network to improve late-life health [7].

The discovery of glycogen synthase kinase 3 as a therapeutic target will lead to more effective treatments that can modulate aging and further improve healthspan. Other study has uncovered tissue-specific responses of cellular processes to lowered IIS. Lowered activity of the insulin/insulin-like growth factor signaling network can ameliorate the effects of ageing [8].

Another diabetic and anti-aging drug is proven to have a preventative effect against COVID [9]. These results show that while diabetes is an independent risk factor for COVID-19-related mortality, this risk is dramatically reduced in subjects taking metformin prior to diagnosis of COVID-19.

Metformin study now shows the effect in non-diabetics COVID patients! In this issue of *Cell*, Wu et al. employed *C. elegans* and human cell experiments to identify a pathway through which metformin increases lifespan and inhibits growth. A key transcriptional target, ACAD10, is activated when metformin induces nuclear exclusion of the GTPase RagC, thereby inhibiting mTORC1 through an unexpected mechanism [9]. A confirmation of metformin effect was demonstrated at the ILA Conference, February 11.

Aging and aging-related diseases, like cardiovascular disease, cancer, diabetes, and neurodegenerative disorders, which have increased exponentially, are

intrinsically related with redox imbalance and oxidative stress. Phytochemicals such as alkaloids, polyphenols and terpenoids activate the same processes as caloric restriction, fasting and exercise, proven to have a boosting effect on immunity [10].

Reactive oxygen species-related research is increasing due to the involvement of reactive oxygen species in aging and aging related atherosclerosis, cardiovascular and neurodegenerative diseases [11]. Quercetin has been shown to stimulate both antioxidant response genes and protein expression in various cell types, and these proteins may prevent damage from subsequent oxidative insults, such as heme oxygenase-1 in RAW264.7 macrophages [12].

The metabolic, molecular, and cellular mechanisms that mediate both improvement in health during aging to diet and genetic variation in the response to diet are being identified [13]. These works are opening the way to dietary and pharmacological rejuvenation of immunity, in order to mitigate both COVID and aging-related diseases. All these technologies will be validated for a COVID technologies rating, the first consensus on the safety/effectiveness, to be produced during Lifetime Award for COVID.

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***Abbreviations*:**

COVID, coronavirus disease.

***Competing interests*:**

The authors declare that they have no conflict of interest.

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About authors

Edward Musinski is founder of Telewellness digital health company and Scientific rating panel comprised of healthcare and longevity experts.

Dr. Gregory M. Fahy is a biogerontologist, cryobiologist and Editor-in-Chief of The Future of Aging. He is Chief Scientific Officer at Twenty-First Century Medicine.

Email: fahy@interveneimmune.com