AGING IS NOT PROGRAMMED. AGING IS A BIOLOGICAL OVERSIGHT NOT A DESTINY
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In conclusion of his extensive literature review in the Cell Cycle journal in 2013 (Cell Cycle 12:24, 3736–3742; December 15, 2013; © 2013) Dr .Mikhail V Blagosklonny postulated that Genetic pseudo-program is a shadow of developmental growth. Genetic programs determine developmental growth and the onset of reproduction. When these programs are completed, they are not switched off. The same signaling pathways, such as Insulin, PI3K and mTOR (mammalian target of rapamycin) pathways drive cellular growth during early development and aging bringing us robustness early in life and diseases later in life. However, only development is programmed for the evolutionary purpose that dictates survival of the fittest. Aging is the result of these earlier programmed processes which were not switched off and aimlessly continued after the developmental purpose was completed. Evolution as determined by Nature, simply selects the brightest flame, the best more effective signaling pathways which when they aimlessly continue after completion, cast the darkest shadow. In the words of George Martin "The brightest flame casts the darkest shadow."

TOR (target of rapamycin) signalling are kinases that sense growth factor, nutrient or oxygen status and promote appropriate changes in cell growth and proliferation, cell survival, and protein synthesis. The PI3K/AKT/mTOR pathway is an intracellular signaling pathway important in regulating the cell cycle. Therefore, it is directly related to cellular quiescence, proliferation, cancer, and longevity.

A number of investigators, Longo VD 2004, Bonawitz ND et al 2007, Powers RW et al, 2006, Blagosklonny MV, 2007, 2009, 2010, 2011, 2012, 2013, and others have experimentally demonstrated how the mTOR signaling pathway that links development and aging, cellular growth and senescence, robust- ness early in life and diseases later in life, puberty and menopause. These investigators have specifically shown that Inhibitors of the TOR pathway, including rapamycin, decelerate chronological aging. Rapamycin decelerates "chronological senescence" in overcrowded cancer cell culture. The same signaling pathways (such as TOR) that are involved in chronological senescence are also involved in metabolic self-destruction of cancer cells. The same pathways are also involved in cellular geroconversion, organismal aging, and age-related diseases.

There are three categories of aging. The non-programmed (stochastic) theories. The Programmed theories and the Quasi-Programmed theories.

Non-programmed or Stochastic theories are based on functional decline which may be purposeful sometimes but not always, explaining the incidence of multiple diseases during aging that may terminate life. Such stochastic theories postulate that in some cases deteriorating mechanisms are purposefully programmed explaining the process of apoptosis in the multicellular organisms. Biological deterioration is mostly caused by random accumulation of damages, errors, and "garbage" due to multiple causes including

but not limited to free radicals or ROS (Reactive Oxygen Species) that are a byproduct of normal metabolism of oxygen. ROS increase dramatically during exposure to heat (like lasers or radiofrequency) or stress, causing significant damage to cell structures, a phenomenon otherwise known as oxydative stress. Stochastic theories establish a link between aging and disease by postulating an inherent vulnerability in aging due to immune deficiency that leads to disease, hence explaining how Death is sometimes caused by non - programmed random processes leading to diseases. Menopause in women in programmed according to these theories and aging can be slowed via cellular repair.

Programmed theories postulated functional decline that is purposeful and programmed, mostly caused by ROS (Reactive Oxygen Species) and Toxicity. According to programmed theories, death is inescapable and menopause in women is programmed. However such theories do not specify the links between aging and disease. For example, the Evolutionary Natural selection of robust individuals is not supported by the reality of aging that is a decades old process of developing age-related diseases such as cancer, hypertension, diabetes, etc that terminate life. What exactly would be the purpose of developing such diseases according to an Evolutionary Natural Selection principle that always chooses the survival of the most adaptive and useful mechanisms inside our bodies? Neither do programmed theories specify the use of our biological energetic resources that repair life that has been documented in hundreds of articles of self-repair, recovery after biological and even neurological damage, on which subject I did my dissertation in 1983 with at least 168 relevant references at that time.

Quasi-programmed aging is clearly non programmed and non-purposeful. It is caused by mechanistic link between mTOR-driven geroconversion, aging, and age-related pathologies, explaining how cellular hyperfunctions eventually lead to organismal death. According to quasi-programmed theory, neither aging nor menopause is programmed, they are merely manifestations of the aging process, which, in turn, is a pseudo-program of developmental growth. Quasi-programmed theory predicts mechanisms of aging that are determined by mechanisms of growth, differentiation, and development. Aging is a shadow. Its shape is determined by the developmental growth. This can be modelled in cell culture, revealing how growth can be converted to aging. The same intracellular signalling pathways that initially drive proliferation, and then differentiation, also stimulate functions in differentiating cells. Cell senescence-associated hypertrophy and hyper-functions are a continuation of growth. The evolutionary theory predicts quasi-programs, like it predicts genes harmful later in life, if they are useful earlier in life. I emphasize that the quasi-program does not exist for its own sake: it is a shadow. Aging has no purpose (neither for individuals nor for group), no intention. Nature does not select for quasi-programs. It selects for robust developmental growth. Accelerated aging is the price for robustness. Although (in some conditions) natural selection works against quasi-programs of aging, it cannot eliminate them without harming development. Genes that drive aging are needed in development. Knockout of PI3K extends lifespan of primary organisms. But this comes at a price: prolonged development. Even further, disruption of the mTOR gene leads to post-implantation lethality. Whereas disruption of S6K1 extends lifespan knockout of both S6K1

and S6K2 causes perinatal lethality. TOR is required for normal growth during larval development.

In conclusion a Quasi-programs are the shadows of growth and development that can be stopped by signalling mechanisms that abolish specific aimlessly running mechanisms that ultimately result in aging and disease such as the PI3K/AKT/mTOR pathway. Under the Quasi-programmed aging model indiscriminate "elimination" of programs or trying to "change" the body will ultimately hurt the body. Pausing specific signalling pathways must be combined with signalling mechanisms involved in self repair, basically combining quasi-programmed and unprogrammed aging theories. Next generation signalling technology can trigger mechanisms that pause certain signalling sequences while filling in missing parts of deteriorated bio-signals, repairing signalling pathways that are essential in body repair. Clinical research supports the conclusion that enhanced signalling communications and suspension of maladaptive signalling sequences can disperse shadows while enhancing natural alternatives or self-repair and systemic purposefulness.