The fight against aging and death

The anti-aging manifesto

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“The problem that I remain the most passionate about is for us to make some real and continued progress in the fight against aging and death. This is not just about my facing the problem, but everybody on this planet faces it, there’s about 100,000 people a day who die, mostly from diseases linked to old age. And so what I always find extraordinary is how little we’re doing about this. It seems that people are either in a mode of denial or acceptance, which are in some ways opposite extremes, but they both have the effect of stopping you from doing anything. If you are in denial and say this is not a problem or if you accept it and say there is nothing you can do about it, both of these are sort of passive modes and I think what we need is a much more active mode. Instead of being in denial and acceptance I’d like us to spend a lot more time fighting death. People always say that death is natural, to which I believe the response has to be there is nothing more natural than to fight death.”

—Peter Thiel
My natural state
A word of caution before we dive in
Consider it all

1. Length of life
2. “Quality” of life
3. Your appetite for risk
4. What you’re willing to give up
Addressing this problem—antiaging and longevity—can be divided into 2 parts

1. Delaying death as long as possible

2. Optimizing the years of life as much as possible
1. Delaying death as long as possible

2. Optimizing the years of life as much as possible
Ten leading causes of death in the United States

- Heart disease: 597,689
- Cancer: 574,743
- Chronic low respiratory disease: 138,080
- Cerebrovascular disease: 129,476
- Unintentional injury: 120,859
- Alzheimer’s disease: 83,494
- Diabetes: 69,071
- Nephritis: 50,476
- Influenza & pneumonia: 50,097
- Suicide: 38,364

If you’re sitting in this room today...

1. **Atherosclerotic disease**
   (i.e., Heart disease, stroke)

2. **Malignancy**
   (i.e., Cancer)

3. **Neurodegenerative disease**
   (e.g., Alzheimer’s disease)
Atherosclerosis, 101

Lipoprotein

Cholesteryl ester

Free cholesterol

Phospholipid

Triglyceride

“Boats”

“Cargo”
The big question in cancer today:

Is cancer a *genetic* disease or a *metabolic* disease?
Differentiated tissue

- $+O_2$:
  - Glucose → Pyruvate → $CO_2$
  - Oxidative phosphorylation: $\sim36$ mol ATP/mmol glucose
- $-O_2$:
  - Glucose → Lactate

Proliferative tissue

- $+/-O_2$:
  - Glucose → Pyruvate → $CO_2$
  - Aerobic glycolysis (Warburg effect): $\sim4$ mol ATP/mmol glucose

Tumor

- $+O_2$:
  - Glucose → Pyruvate → Lactate
  - Anaerobic glycolysis: $2$ mol ATP/mmol glucose
- $-O_2$:
  - Glucose → Lactate
  - or
  - Glucose → Pyruvate → $CO_2$

Lactate
T – tumor in liver (pre- and post-therapy)
K – kidney (does not contain tumor but concentrates FDG)
Brian metabolism, 101
Is there a common thread running through the "big 3" killers?

Obesity → Insulin resistance → Metabolic diseases → Premature death

- Stroke
- Atherosclerosis
- Gall bladder disease
- Type 2 diabetes
- Hypertension
- Neurodegeneration
- Sleep apnea
- Asthma
- Fatty liver disease
- Osteoarthritis
- Cancer
If you avoid **insulin resistance**, you minimize the risk of **metabolic diseases**

1. **Diet** (Two big ideas to consider)
2. **Sleep** (Think about your ancestors)
3. **Exercise** (More on this later)
4. **Stress reduction?** (Probably)
5. **Micronutrients?** (Maybe)
6. **Avoid toxins?** (Obviously)
1. Delaying death as long as possible

2. Optimizing the years of life as much as possible
Getting older usually means...

1. Getting **slower**

2. Getting **weaker**
   (and more prone to injury)

3. Getting **colder**

4. Getting **fatter**

5. Being **less energetic**
Fix the hormones...

Hypothalamus (brain region controlling the pituitary gland)

Pituitary gland (secretes many different hormones, some of which affect other glands)

Thyroid gland (affects metabolism, among other things)

Parathyroids (help regulate level of calcium in the blood)

Adrenal glands (help trigger the fight-or-flight response)

Pancreas (regulates the level of sugar in the blood)

Testis (secretes male sex hormones)

Ovary (secretes female sex hormones)

...and you begin to approximate fixing the person
My thoughts on exercise

1. Constant “cardio” may accelerate inflammation, aging
2. Lots of time sub-threshold → RHD → Afib (and sometimes Vfib)
3. Preserve muscle mass as much as possible (men AND women)
4. To achieve #3 requires a very deliberate type of exercise *(Hint: most people never come close)*
5. Reduce activities that increase orthopedic injury as you age
6. Maintain joint integrity and flexibility (dynamic >> static)
7. If you can afford it, quality tissue work does wonders
8. Never forget two things about our species...
But what about [fill in the blank]...?

1. Your genes matter more than anything else when it comes to longevity (by a lot).

2. Most “magic bullets” (e.g., resveratrol) turn out to be of no efficacy whatsoever.

3. Caloric restriction is probably the greatest action one can take to impact longevity (shy of choosing long-living parents). The big question is why. Is it the actual number of calories or the reduction in the type of calories that raise insulin and IGF?

4. If any class of drug being evaluated today is going to have an effect on longevity (not sure that will happen), it’s probably a drug that inhibits mTOR (e.g., rapamycin).