

**EPITALON:**

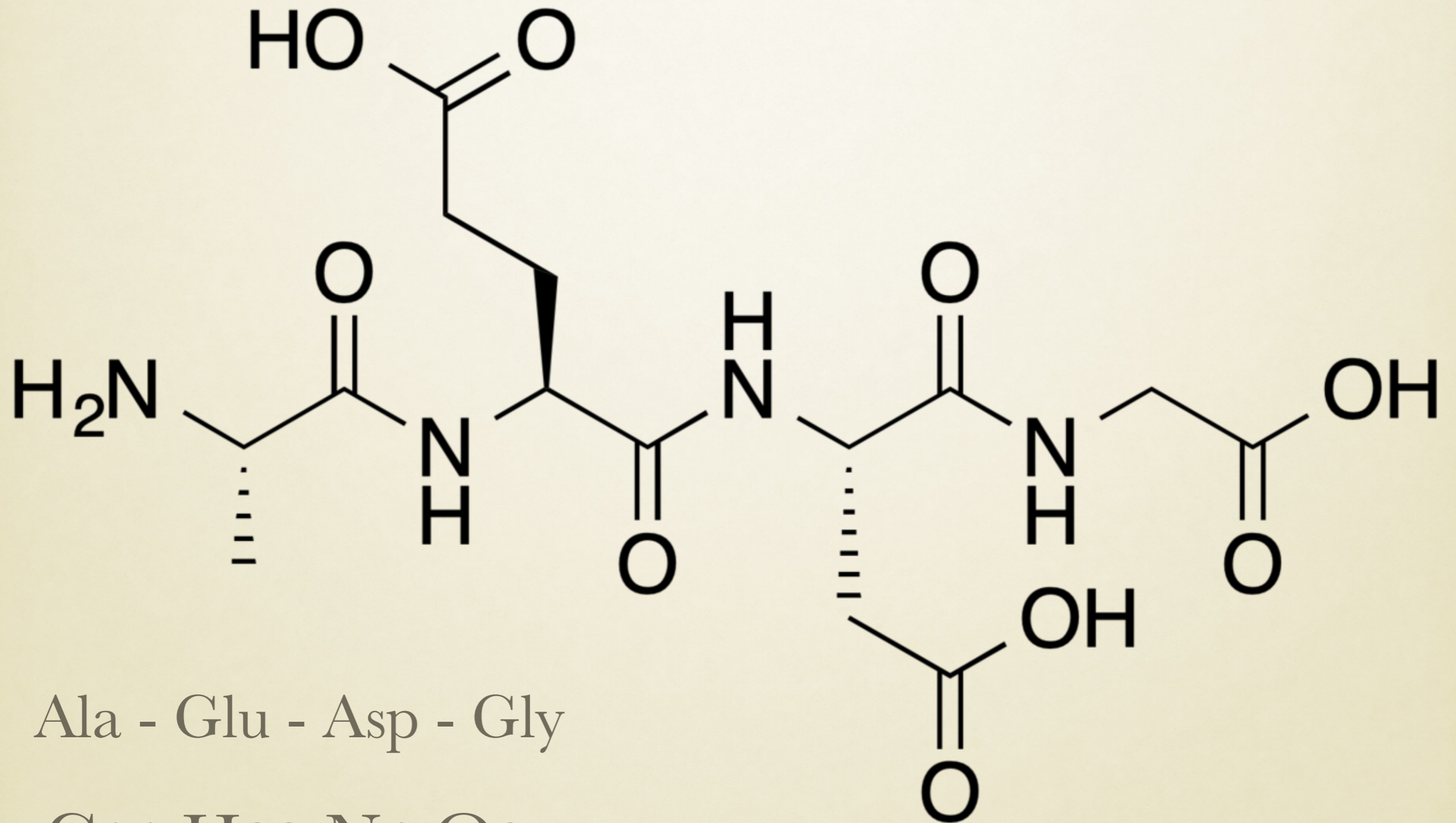
**THE MOST IMPORTANT  
THERAPY IN FUNCTIONAL  
MEDICINE?**

**JAMES RANIOLO, DO, AOBFP, ABAARM, FAARFM**

**FOUNDER, WYOMING CENTER FOR OPTIMAL HEALTH**

**FOUNDER, AMERICAN VITALITY ASSOCIATION**

Epithalamin = Epitalon?



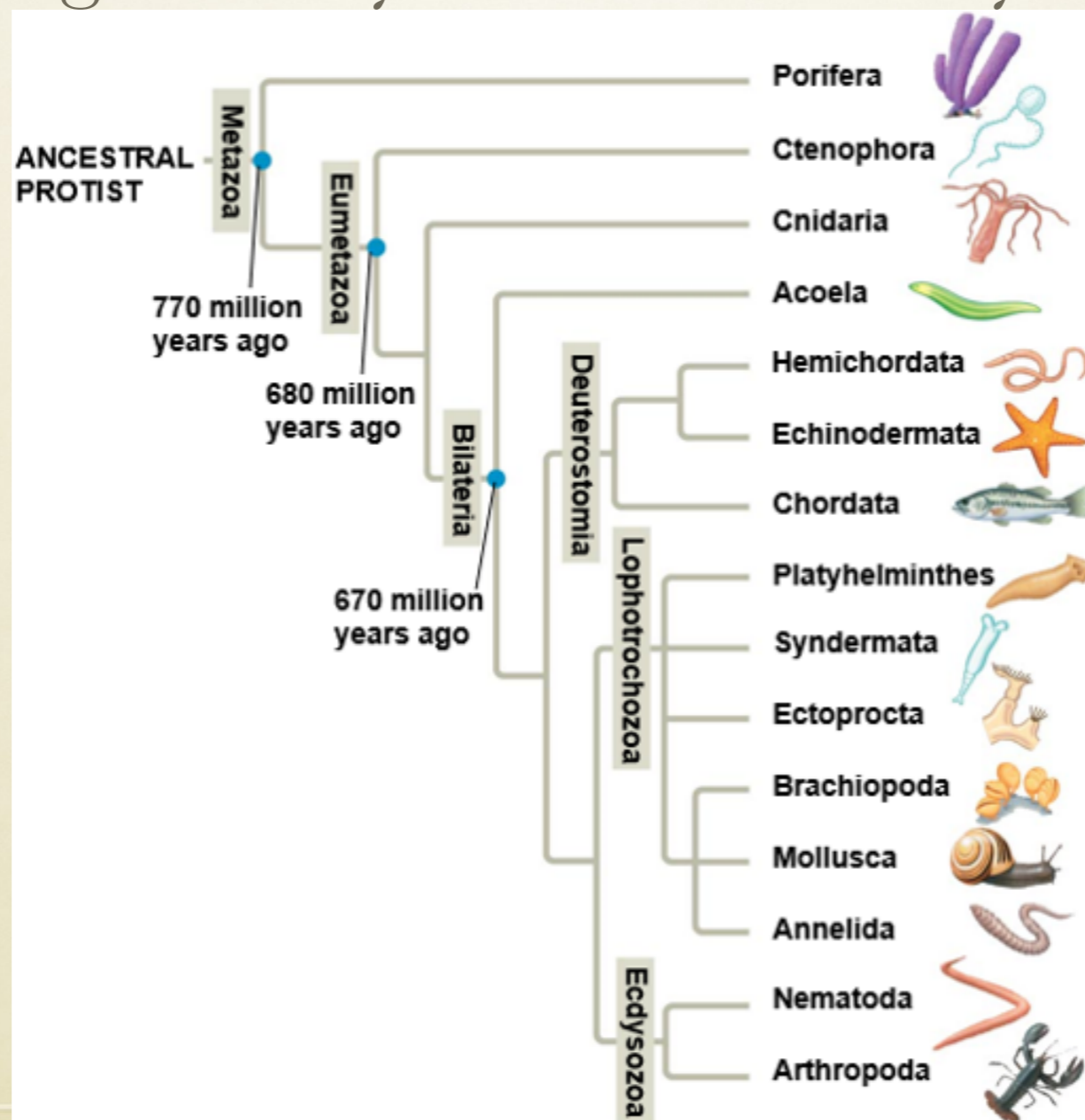
Ala - Glu - Asp - Gly

C<sub>14</sub>-H<sub>22</sub>-N<sub>4</sub>-O<sub>9</sub>

# “THE MASTER PEPTIDE”

## OF THE MULTICELLULAR ANIMAL KINGDOM

Epitalon may be the most important and evolutionarily conserved peptide in multicellular animals on this planet, evolving as early as 770 million years ago.



Epitalon coordinates cell cycles and stimulation of cell division

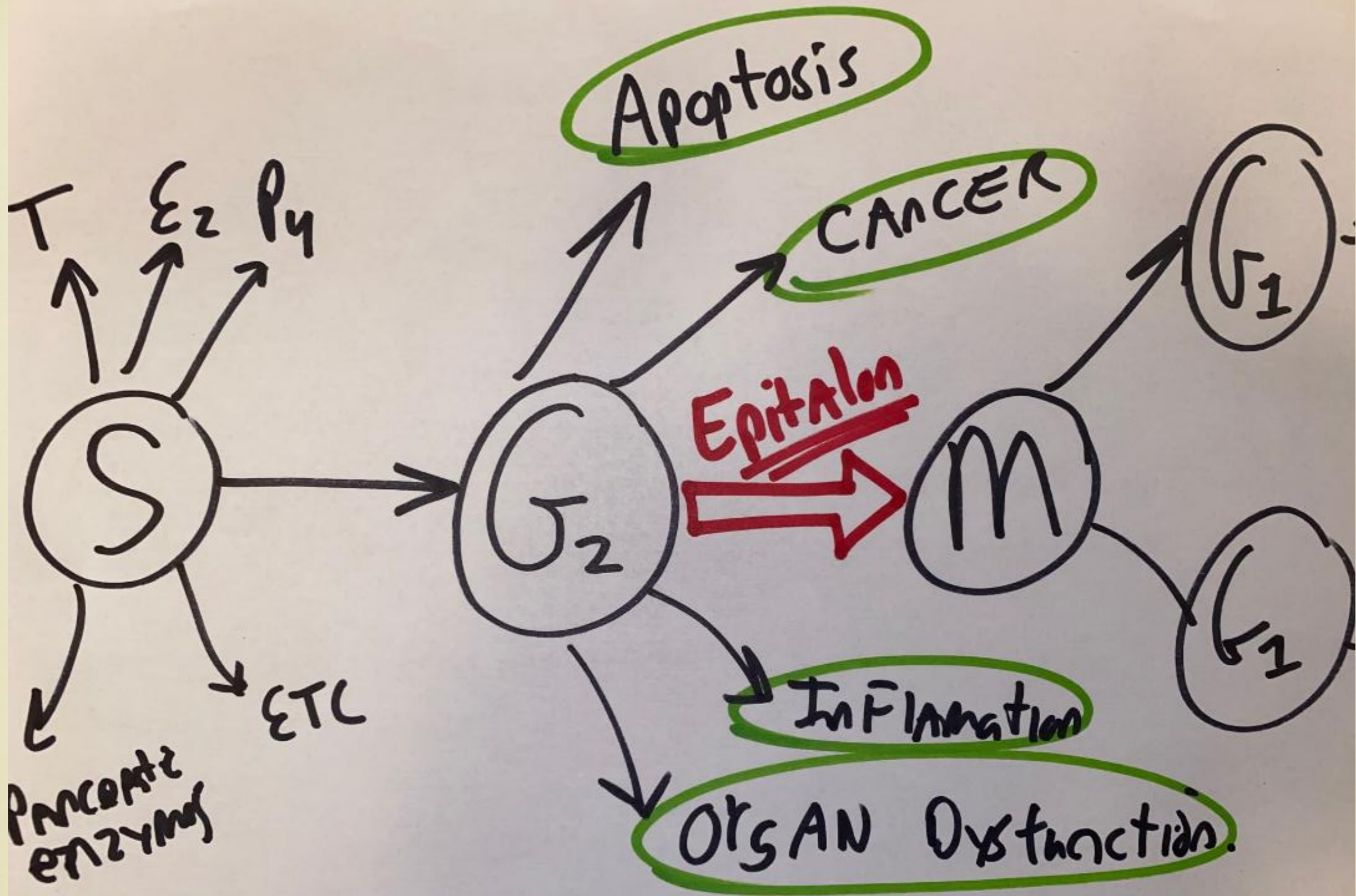
**No epitalon? Cell cycle “arrest” may occur.**

Without epitalon for more than 2.5 years, cells are more likely to enter into a state of perpetual cell cycle arrest, also known as **cellular senescence**.

# MECHANISM OF ACTION:

“These results indicate that in human somatic cells Epithalon can induce the expression of telomerase enzyme component, telomerase activity, and telomere elongation (by on average 33.3%).”

Epithalon Peptide Induces Telomerase Activity and Telomere Elongation in Human Somatic Cells  
V. Kh. Khavinson, I. E. Bondarev, and A. A. Butyugov  
Translated from Byulleten, Eksperimentalnoi Biologii i Meditsiny, Vol. 135, No. 6, pp. 692-695, June, 2003;  
Original article submitted April 24, 2003



# EFFECTS ON LIFESPAN?

Lab animals given epitalon live on average 25% longer...

(even JELLYFISH and CRUSTACEANS and FRUIT FLIES given epitalon live 25% longer!)

How much longer **COULD** humans live with regular doses  
of epitalon ?

# HAYFLICK LIMIT:

- In Human cells, 34 cell divisions is considered to be the “Hayflick Limit” where telomere length becomes too short to allow further mitotic events
- When exposed to Epitalon throughout their lifecycle; human tissues are known to extend their Hayflick limit to 44 cellular divisions... around a 25% increase.

Peptide Promotes Overcoming of the Division Limit in Human Somatic Cell  
V. Kh. Khavinson, I. E. Bondarev, A. A. Butyugov, and T. D. Smirnova  
Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 137, No. 5, pp. 573-577, May, 2004  
Original article submitted January 24, 2004



## THE UNPROVEN MATH OF EPITALON LIFE EXTENSION:

- (Typical cell cycle length) X (Hayflick limit)= expected age
- $2.5 \times 34 = 85$  (the average age of death in Humans)
- $2.5 \times 44 = 110$  (the age of the oldest Humans)
- **Is this a coincidence?**

# PHILISPOHICAL QUESTIONS...

- Why do totally **healthy** organisms exposed to large intermitant doses of Epitalon experience life prolongation?
- Is this a way to keep the most “valuable” members of a species around the longest?
- Is this simple and fortuitous discovery that supraphysiological doses of epitalon increase Hayflick limits and extend lifespan?
- Are any diseases associated with low epitalon levels? and if so; why? (the answer of course... is of course)

**TWO “DISTINCT” PHYSIOLOGICAL ROLES...**  
**TWO “DISTINCT” CLINICAL ROLES FOR EPITALON**

- **Health preservation and wellness:** (Via telomere elongation)  
Even in healthy clients when normal cellular division occurs in the presence of epitalon; it lengthens telomeres allowing for an increase in Hayflick limit and may extend lifespan and healthspan...
- **Therapeutic use for patients with symptoms or evidence of organ dysfunction:** (Via alleviation of cell cycle arrest)  
“Epitalon induces a cessation of cell cycle arrest and helps resolve cellular senescence; improving the efficiency and health of cells, tissues, and organs.”

# SMALL SCALE RUSSIAN STUDIES... USING EPITHALAMIN (NOT EPITALON)

Biogerontology (2010) 11:139–149  
DOI 10.1007/s10522-009-9249-8

RESEARCH ARTICLE

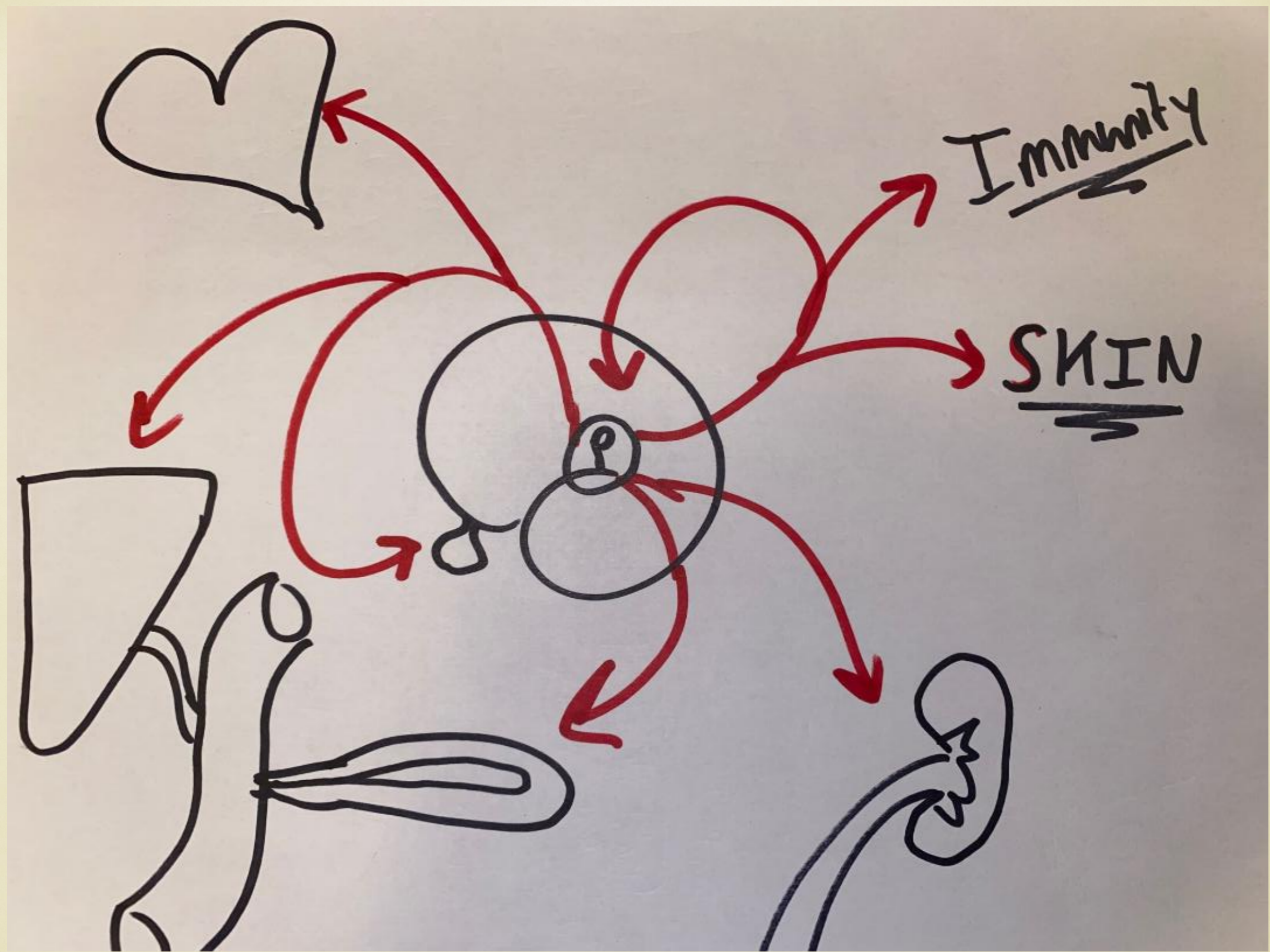
## Peptide bioregulation of aging: results and prospects

Vladimir N. Anisimov · Vladimir Kh. Khavinson

**Table 3** Effect of treatment with peptide preparation on mortality rate in elderly and old subjects

Group of subjects	Indices	Control (administration of polyvitamins)	Administration of the pineal gland preparation	Administration of the complex of thymus and pineal gland preparations
Elderly people (60–74 years)	Number of subjects	48	46	No studies
	Initial mean age (years)	69.3 ± 2.2	71.1 ± 1.4	
	Mortality rate in the course of 8 years (%)	13.6	8.5*	
	Mortality rate in the course of 12 years (%)	44.1	22.3*	
Old people (75–89 years)	Number of subjects	22	24	20
	Initial mean age (years)	80.2 ± 1.6	81.5 ± 2.1	82.1 ± 2.3
	Mortality rate in the course of 6 years (%)	81.8	45.8*	33.3*

\*  $P < 0.05$  as compared to the control



# USE IN PANCREATIC INSUFFICIENCY

(OR HOW I FELL IN LOVE WITH EPITALON)

- **A common presentation to my clinic:** Patients with a host of symptoms which may include fatigue, malaise, declining school performance, possible chronic gastrointestinal problems and floating stools been to multiple physicians with no diagnosis... easily diagnosed with pancreatic Insufficiency with a simple stool test showing low pancreatic elastase and steatorrhea, and treated on pancreatic enzymes with resolution of presenting complaints.
- Typical workups for these clients involve screening for and treating underlying causes of pancreatic insufficiency (r/o **chronic subclinical pancreatitis**, assess **Cystic fibrosis carrier status** and other genetic contributing factors like **MUC and other gene abnormalities**, as well as **autoimmune** and **mitochondial abnormalities**)
- In a certain percentage of clients after extensive workups and therapeutic trials I had not been able identify any causative pathology, no matter how hard that I looked...

## CLINICAL EXPERIENCE OF USING EPITALON FOR EARLY ONSET PANCREATIC INSUFFICIENCY:

- Out of at least 7 personal clients with early onset and unexplained Pancreatic Insufficiency, 5/7 had improvement in condition (elevated fecal pancreatic elastase, reduce dosage of digestive enzymes)
- 3 had resolution of symptoms; with near normalization of pancreatic elastase levels and no further need to continue on pancreatic enzymes.
- All of these clients had significant die-off reactions (acne/rashes, malaise, fatigue, cognitive symptoms) and a subsequent improvement of baseline functioning afterward... and all had improvements on other aspects of health as well (senescence was apparently widespread and not just pancreatic)
- **Epitalon allows clinicians to potentially reverse diseases that other wise have no other therapeutic options.... as it can address the core underlying problem.**

# IS YOUR CLIENTS RENAL DISEASE BEING CAUSED BY CELLULAR SENESENCE?

- After years of trial and error, significant improvement in renal function have remained elusive to me, and with rare exception the best that I learned to hope for was cessation of functional kidney loss
- On a stable client who has been metabolically and nutritionally optimized with stable eGFR's; It is quite typical to see a boost of eGFR in my clients of 15% after the first course, and another 5% if repeated in 6 months.



# IS YOUR CLIENTS HEPATIC DYSFUNCTION BEING CAUSED BY CELLULAR SENESCENCE?

- Frequently see normalization of Thyroid conversion (normalized ratios of [T4:T3])
- Often see improvements of hepatic estrogen metabolization... even on nutritionally optimized patients (reduced SHBG and secondary estrogen metabolites; reduced need for I3C/DIM/SamE)
- Often see improvement of Glutamate toxicity symptoms and/or reduced need for Oxyloacetate supplementation to control Migraine, PMS/PMDD or insomnia.
- “Glutathione” clients often have significant reduction in need for further glutathione supplementation

# IS YOUR PATIENTS HEART FAILURE BEING CAUSED BY CELLULAR SENESCENCE?

- One single Case report to share: Over summer wife brings in a 76 year old cowboy with global decline over two years (to sick to go elk hunting)
- %: SOB, DOE, leg weakness, and he has trouble seeing the crosshairs of his rifle scope, 1-2+ pitting edema on exam. He really wants to go elk hunting with his mule, Elroy.
- Labs show “cardio-renal syndrome”; eGFR 50, BNP 527 (no hx ASCVD after w/u), and has known macular degeneration
- Essentially refuses any major change to his diet, will only take a few supplements
- Placed on Epitalon x 5 once weekly and a few supplements
- 3 months later his eGFR is 57, BNP is 174, low vision improved, edema all but resolved, and he can now walk uphill
- The cowboy (and Elroy) spent two weeks in Elk camp high up in the mountains and shot an elk and packed it out.



## MY PERSONAL APPROACH TO ADRENAL INSUFFICIENCY HAS CHANGED OVER A DOZEN YEARS:

- Level 1: Adrenal supplements and life style changes (usually takes over a year)
- Level 2: Adding LDN to above or instead of above (usually takes 6 months)
- Level 3: Starting with Epitalon, and only resorting to the above if is ineffective (sometimes fully resolved in two months with no other changes)

### **Regulatory Effect of Epithalon on Production of Melatonin and Cortisol in Old Monkeys**

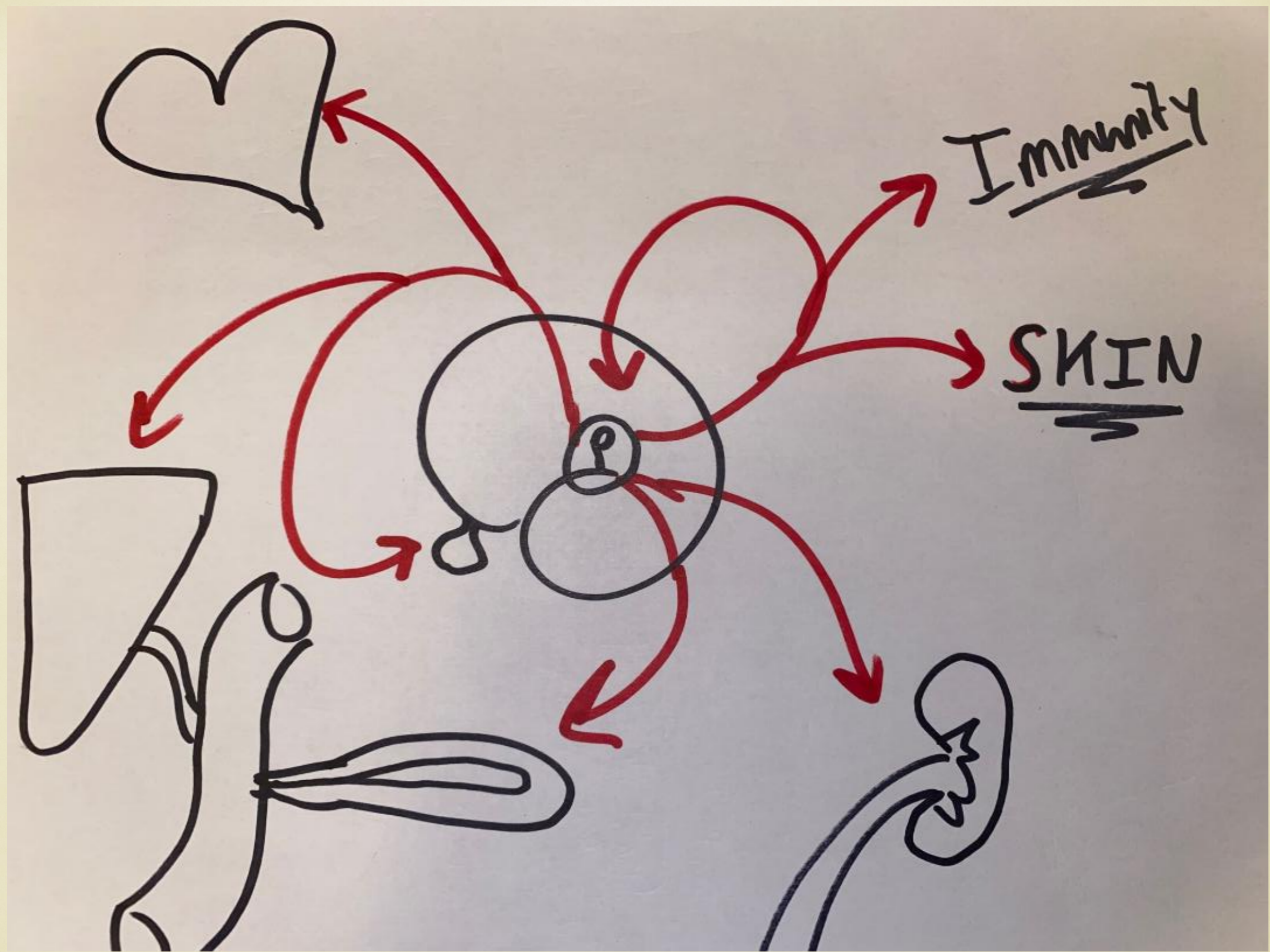
**N. D. Goncharova, B. Kh. Khavinson\*, and B. A. Lapin**

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 131, No. 4, pp. 466-468, April, 2001  
Original article submitted February 28, 2001

Epithalon not only stimulated melatonin synthesis in old monkeys, but also normalized circadian rhythms of peripheral blood cortisol concentration (Fig. 1, *b*). Cortisol content in old animals did not drop in evening (21.00), which indicated a decrease in the amplitude of its circadian rhythms (similarly to humans [12]).

# PRIMARY VS SECONDARY HYPOGONADISM IN MEN

- **Level 1:** Give them all TRT; just need to decide on the best delivery system.
- **Level 2:** Screen for those with secondary hypogonadism, if present supplement to improve secondary estrogen metabolization (if needed) and augment HPA response with a variety of substances (HCG, Clomiphene, etc)
- (Those with Primary Hypogonadism are still stuck on TRT)
- **Level 3:** Epitalon may, in some cases, improve function in BOTH; Improves HPA axis function as well as Testicular ability to secrete Testosterone.
- (Those with Primary Hypogonadism sometime don't need TRT)



**TO WHAT EXTENT ARE THE COMMON SYMPTOMS EXPERIENCED BY YOUR CLIENT BEING CAUSED BY CELLULAR SENESCENCE?**

- Perhaps the easiest way to find out is to give a course of epitalon. Then wait and see, they will tell you.
- What they tell me is often a surprise and I never would have predicted

## WHAT OTHER SYMPTOMS MAY BE BEING CAUSED BY CELLULAR SENESCENCE IN YOUR CLIENTS?

- **“Nothing has changed”:** Not uncommon to have this reported
- **Feelings of well being and physical robustness:** very commonly reported
- **Tinnitus:** frequent reports of 50% or more reduction of chronic tinnitus (80% after second dose!)
- **Skin:** frequent reports of improvement in skin texture, resolution of rashes or skin lesions
- **Peripheral edema:** multiple reports of improvement or normalization
- **Neurological:** Reduced neuropathy, better balance, quicker reflexes
- **MS:** Multiple reports of better balance and subjective lessening of symptoms after a single course
- **Dyspareunia:** one report of total resolution after 9 years of constant pain onset after childbirth, multiple reports of improved vaginal lubrication with less need for estriol suppositories or lubricants
- **Improved libido or sexual function:** often experienced even with no change of labs

# PHILOSOPHICAL CHANGE OF APPROACH SINCE USING EPITALON CLINICALLY

- My **Old school** approach: Use nutritional supplementation to help maximize the efficiency of dysfunctional cells that I now recognize as being senescent (with clients stuck on multiple supplements and complex regimens for years)
- My **New School** approach: Offer Epitalon as a way of resolving cellular senescence in patients when it can be reasonably suspected, then use minimal nutritional supplements to reach goals



“DOCTOR, FOR THE LEAST AMOUNT OF MONEY SPENT, AND THE LEAST AMOUNT OF EFFORT PUT FORTH, WHAT IS THE NUMBER ONE THING THAT I CAN DO TO IMPROVE MY HEALTH AND INCREASE MY POTENTIAL LIFESPAN?”

- This is the questions our patients SHOULD ask of us.
- If anyone has a better answer than “**Take a course of Epitalon every year**”... PLEASE let me know.

# DOSING PROTOCOLS:

- 1 ml SQ every three days for 5 doses total (over 15 days) should eliminate most cellular senescence... taking more has no proven benefit.
- Benefits can be seen for SEVERAL YEARS after the last dose is taken.
- When to repeat is subject to the law of diminishing returns: No or minimal benefit for SENESENSE if given before 6 months.
- Taking every 6 months vs annually: 20% ROI vs annual dosing?
- My protocol: If a benefit was seen, suggest another course every 6 months until stable baseline. Otherwise, suggest yearly.
- Other dosage protocols: Please send me the evidence.

WHY DOES  
“**EPITALON DEFICIENCY SYNDROME**”  
OCCUR?

- Obvious: Head injury clients; often with SPECT scans showing injury in the area of the Pineal gland, but suspect injury to other areas also may inhibit secretion
- Pure speculation: Chronic stress? Environmental toxicity? **Genetic predisposition? EMF exposure (direct vs indirect?)** Other?



THIS CHRISTMAS...

DON'T FORGET TO INJECT YOUR EPITALON

[drraniolo@yahoo.com](mailto:drraniolo@yahoo.com)