





# ANGIOGENESIS

"Angiogenesis during exercise and training"

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# WHAT IS ANGIOGENESIS?

## Definition and Basics

The term angiogenesis is derived from the root words angio, meaning blood, and genesis, meaning formation. The term lymphangiogenesis refers to the formation of both new blood vessels and lymphatic vessels.

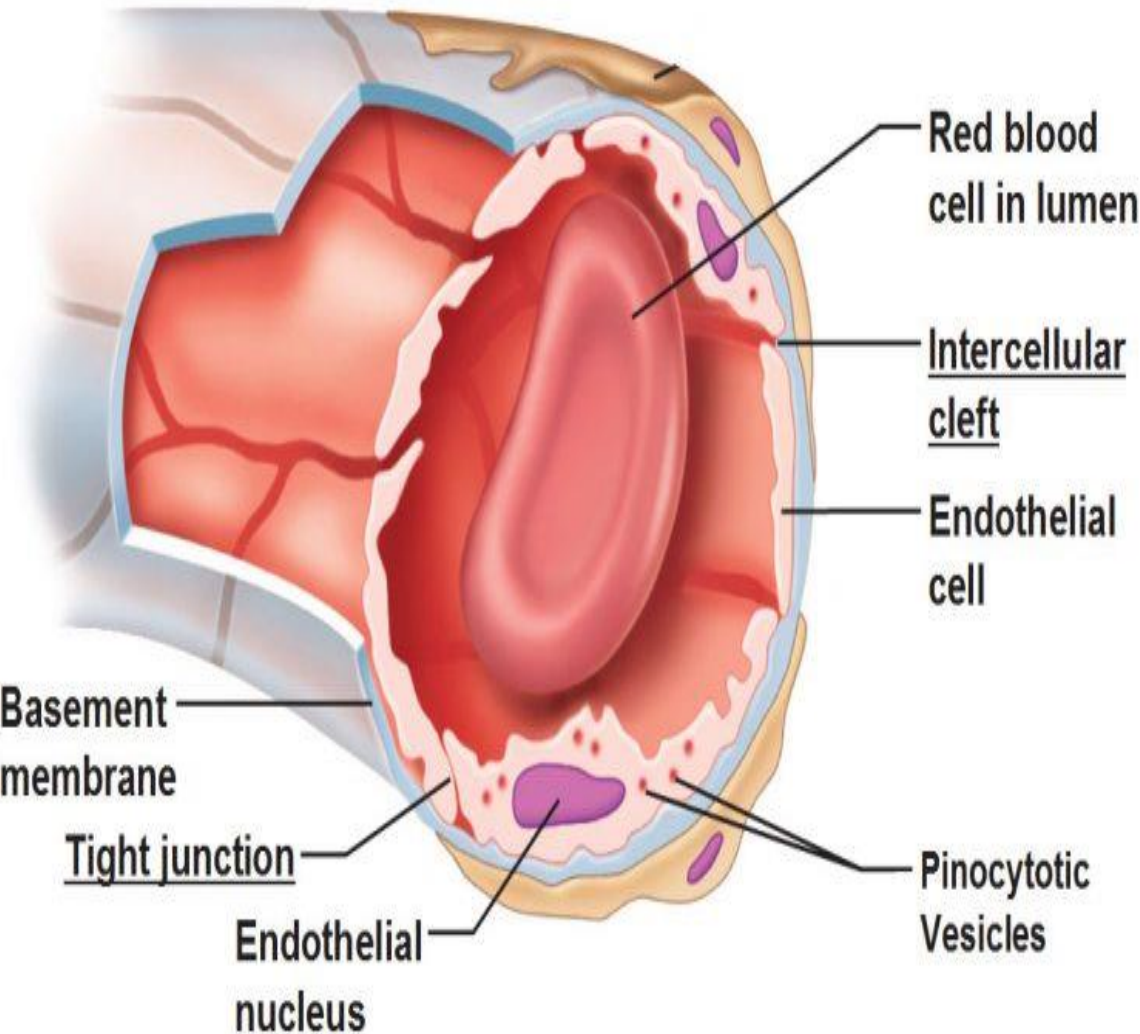




## GOOD VS. BAD ANGIOGENESIS (NORMAL VS. ABNORMAL)

As with many processes in the body, however, there is a delicate balance. With cancer, this formation of new blood vessels (angiogenesis) is what allows tumors to grow.

Structure of Capillaries: Continuous Capillary has many Tight Junctions with spaces called Intercellular Clefs for passage of small molecules



(a) **Continuous capillary.** Least permeable and most common (e.g., skin, muscle).

# CAPILLARY

## STRUCTURE OF CAPILARITY

**Different structures of capillaries determine the degree of permeability**

Function and structure are very intimately tied in together.

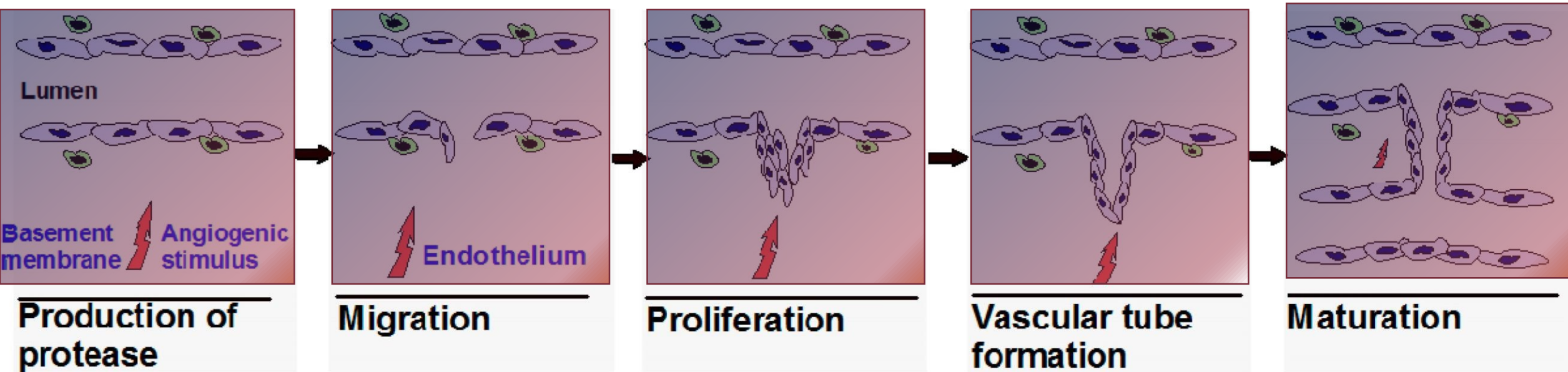
This is called a **Continuous Capillary**. The spaces in between the individual endothelial cells are loaded with **tight junctions** holding the cells together of a continuous type of capillary. The spaces in between that allow things to pass through are called **intercellular clefts** that are not totally sealed but very tiny making these the least permeable capillaries and most common. This is found in skin and **muscle**, sort of like a standard issue capillary.

# THE PROCESS OF ANGIOGENESIS

Involves Several Steps

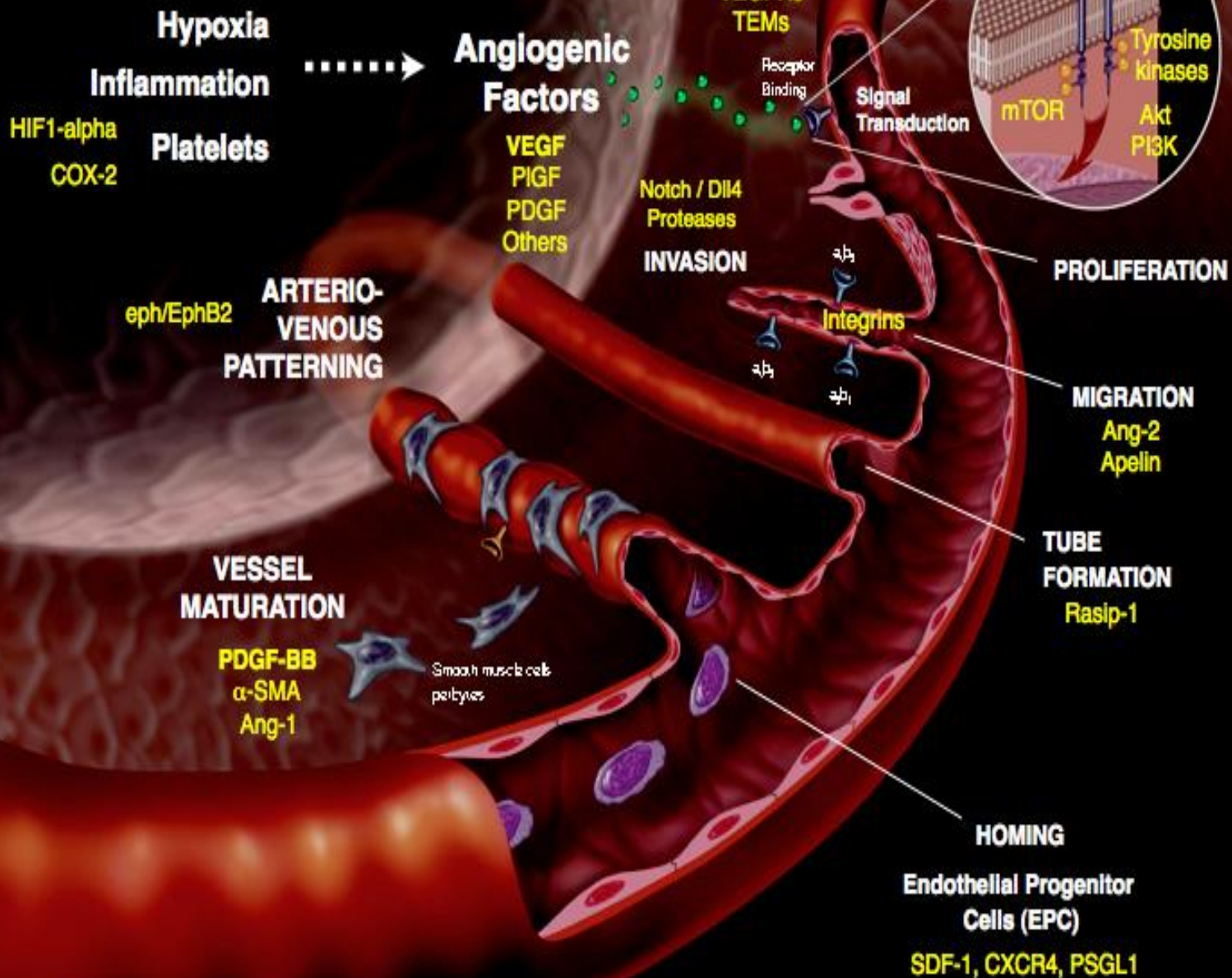
The process of angiogenesis involves several steps involving endothelial cells (the cells that line the vessels). These include:

- Initiation: The process of angiogenesis must be activated by some signal (prior to this, it's thought that the blood vessels must dilate and become more permeable)
- Sprouting and growth (proliferation)
- Migration
- Tube formation
- Differentiation (maturation)





# Multiple targets in angiogenesis

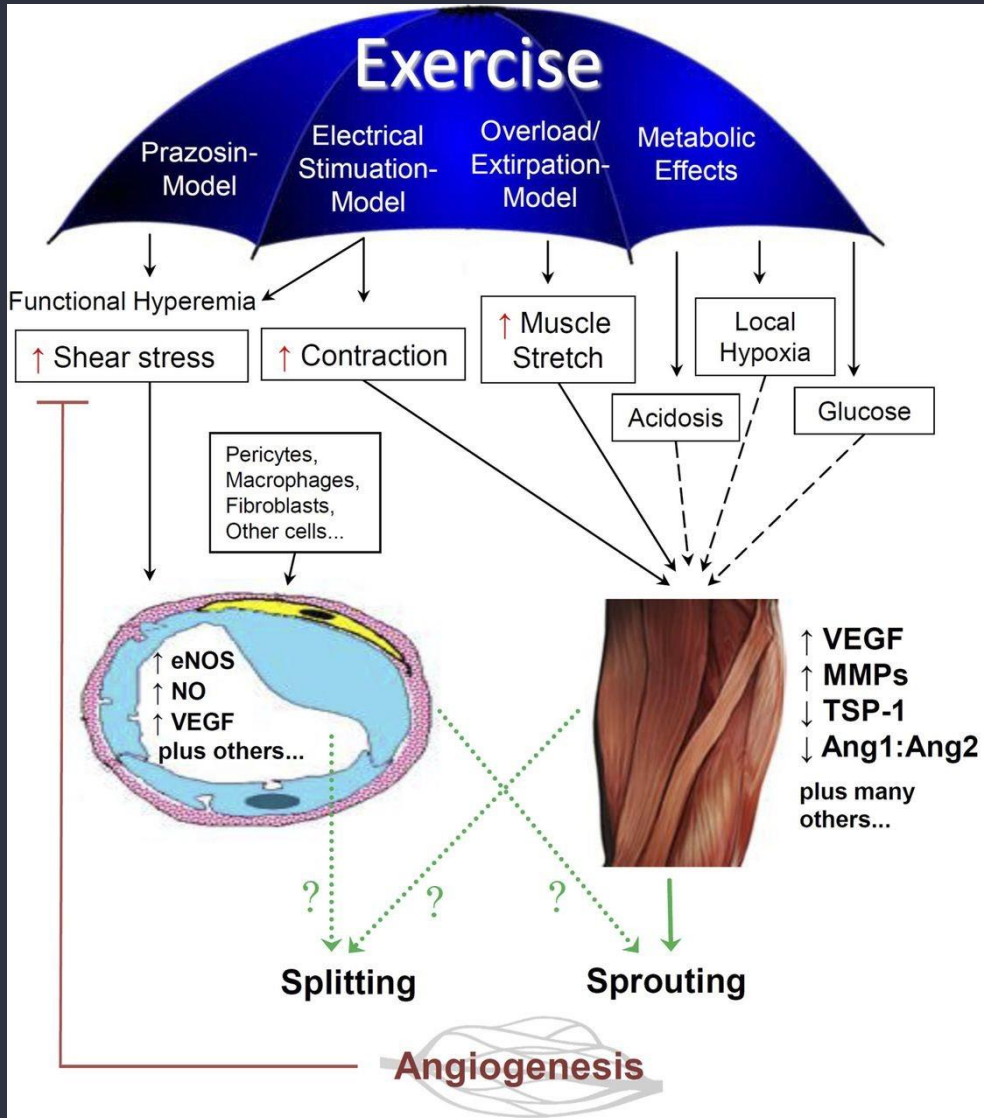


# THE MAIN ADAPTATIONS TO AEROBIC TRAINING?

Muscle capillary density

Not all people aspire to be endurance athletes, but all people do value the freedom associated with being able to take care of themselves. People engage in training to enhance functional capacity, be it to improve physical performance or simply to improve quality of life

# ADVANCES AND CHALLENGES IN SKELETAL MUSCLE ANGIOGENESIS



## EXERCISE

PRAZOSIN MODEL

ELECTRICAL STIMULATION MODEL

OVERLOAD/ EXTIRPATION MODEL

METABOLIC EFFECTS

**CONTRACTION**

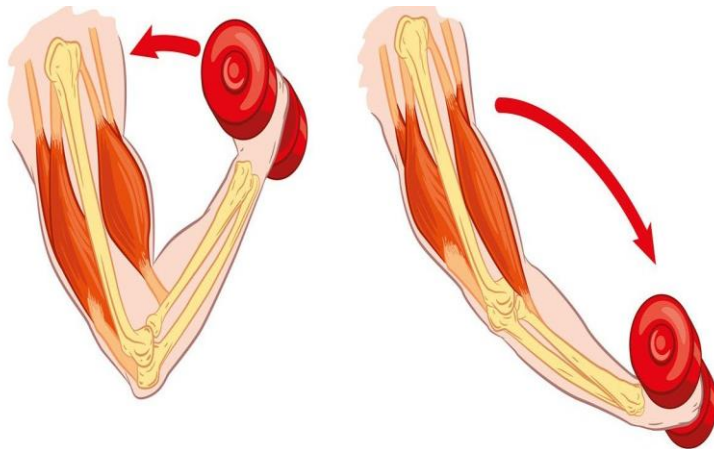
**SHEAR STRESS**

**MUSCLE STRETCH**

**LOCAL HYPOXIA**

# EXERCISE ADAPTATION

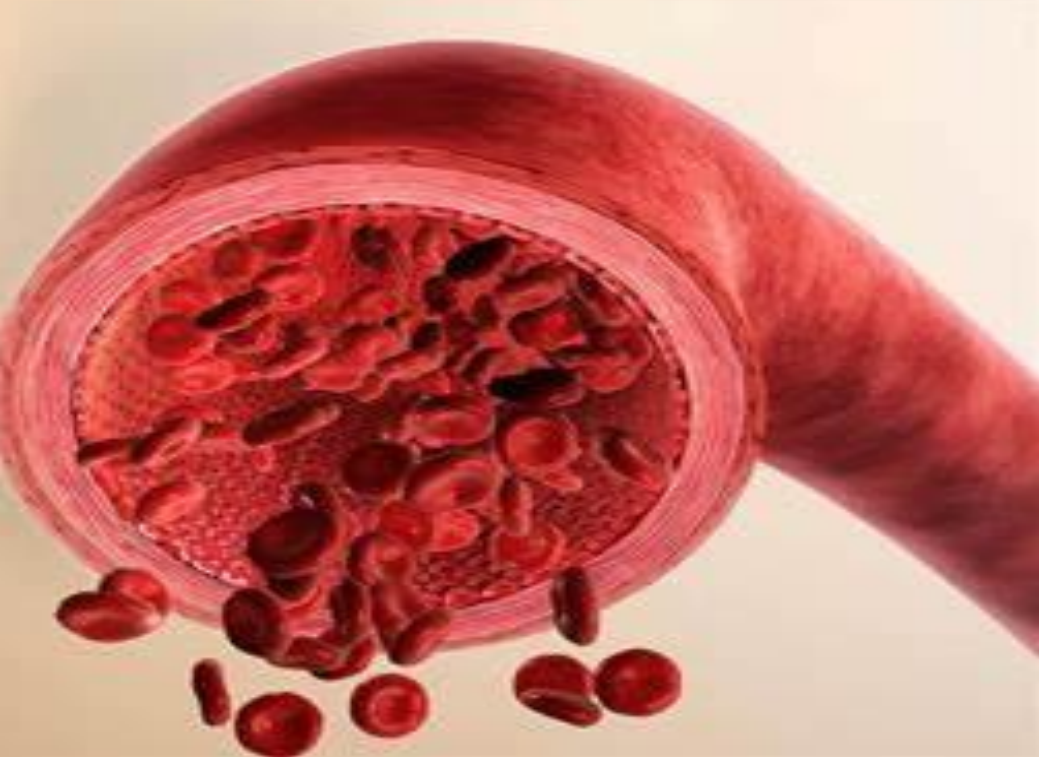
## MUSCLE STRETCH



The average maximal knee-extensor work rate increased 33% from the untrained to the trained state (Table 1). This was accompanied by a 34% increase in skeletal muscle  $VO_{2\max}$  after training (Table 1). This increase in  $VO_{2\max}$  was achieved by a small (9%) but significant increase in muscle blood flow and a large increase in maximal  $O_2$  extraction (21%; Table 1). Maximal  $O_2$  conductance also increased significantly (34%), whereas calculated mean capillary  $PO_2$  remained unchanged. CSA, an indicator of mitochondrial capacity, increased 18.2% from the untrained to trained state (Table 1). Structural changes in the muscle sampled before and after the training period were consistent with knee-extensor training demanding a strength component, resulting in an increase in fiber area (18%). There was also a significant angiogenic response, with an 18% increase in the number of capillaries around each muscle fiber. However, because both fiber area and the number of capillaries/fiber increased similarly, capillary density was unaltered. In combination, these data clearly illustrate that the 8-wk training regimen resulted in significant improvements in  $O_2$  transport through increased capillarity,  $O_2$  conductance,  $O_2$  extraction, and muscle blood flow, all of which translate to a large increase in skeletal muscle  $VO_{2\max}$ .

Exercise adaptation attenuates VEGF gene expression in human skeletal muscle  
R. S. Richardson, H. Wagner, S. R. D. Mudaliar, E. Saucedo, R. Henry, and P. D. Wagner





# *VASODILATORS*

## *AND*

# **SHEAR STRESS**

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Some herbs or supplements can also help with vasodilation. Some supplements have adverse medication reactions, so speak with your provider before taking any herb or supplements. Vasodilator supplements may include:

Cocoa.

Coenzyme Q10 (CoQ10).

Garlic.

L-arginine.

Magnesium.

Niacin (vitamin B3)

# WHAT TO KNOW ABOUT NITRIC OXIDE SUPPLEMENTS

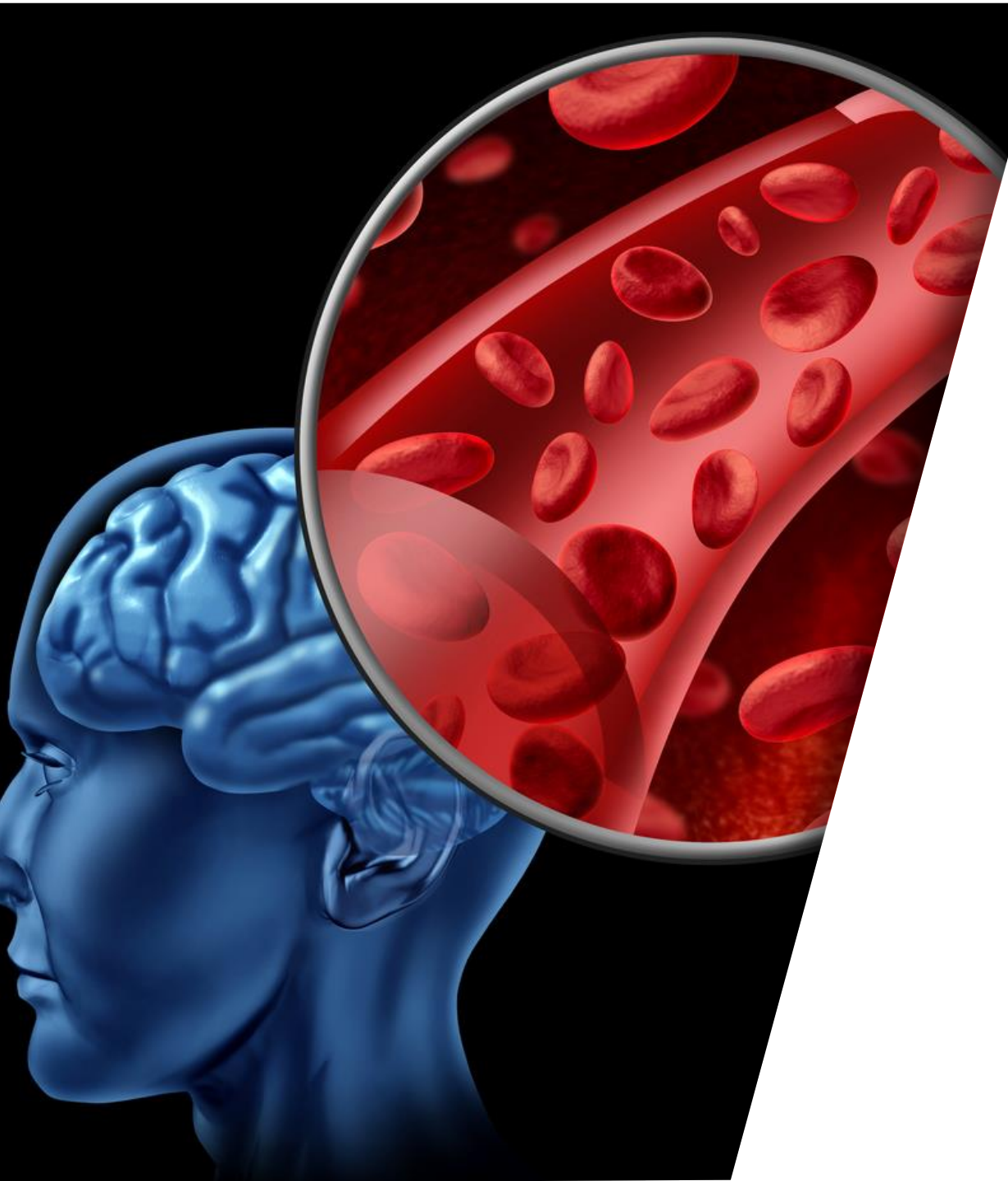


## BENEFITS

- Improves heart health
- Enhancing exercise and recovery
- Reducing high blood pressure in pregnancy

## RISKS

- diarrhea
- stomach pain, bloating, or heartburn
- headache
- heart palpitations
- nausea



# HYPOXIA

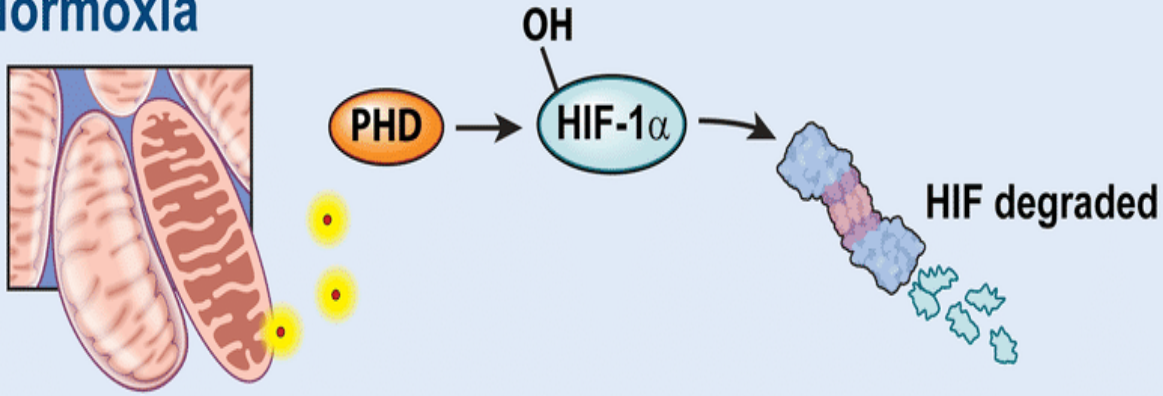
Hypoxiation, lack of, low blood oxygen, oxygen starvation

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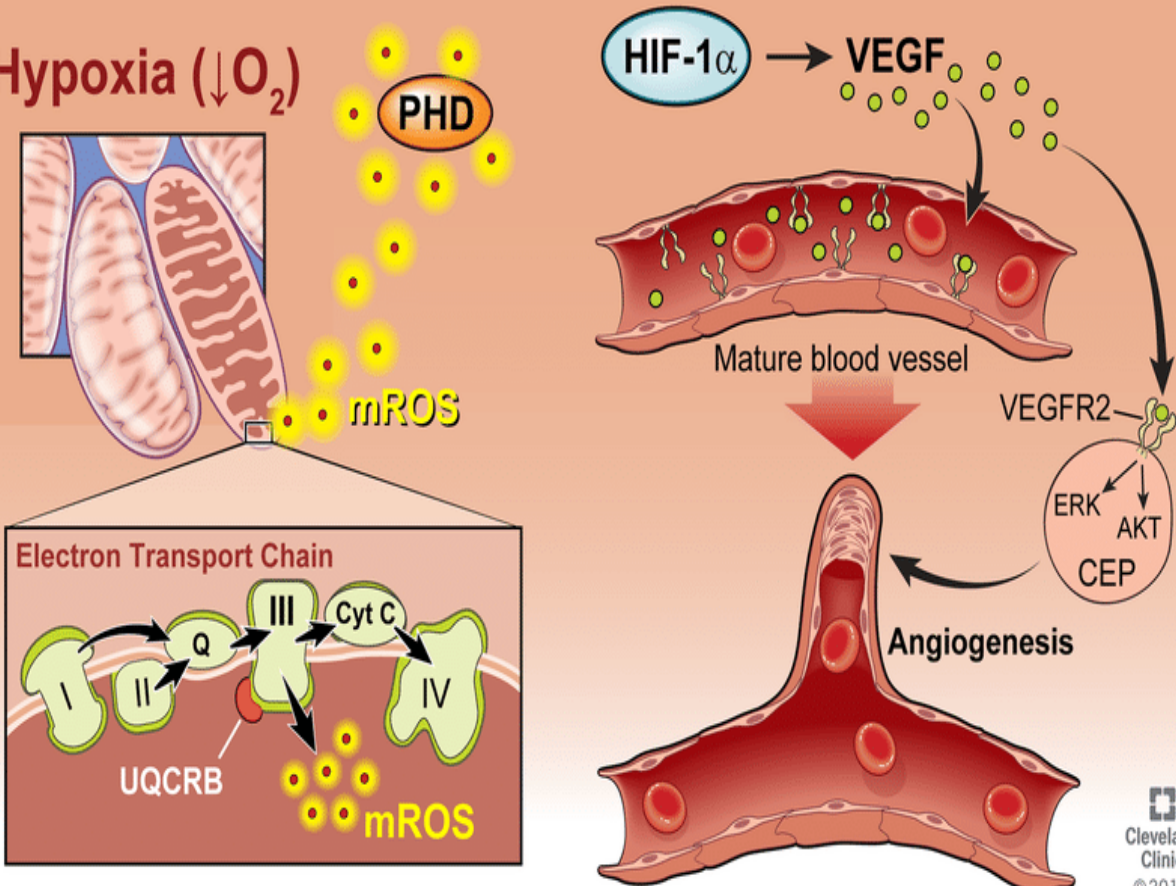
Hypoxia is a condition in which the body or a region of the body is deprived of adequate oxygen supply at the tissue level. Hypoxia may be classified as either generalized, affecting the whole body, or local, affecting a region of the body. Although hypoxia is often a pathological condition, variations in arterial oxygen concentrations can be part of the normal physiology, for example, during hypoventilation training or strenuous physical exercise.



## Normoxia



## Hypoxia ( $\downarrow O_2$ )



# HYPOXIA HIF & VEGF

Angiogenesis extends pre-existing blood vessels to improve oxygen and nutrient delivery to inflamed or otherwise hypoxic tissues. Mitochondria are integral in this process, controlling cellular metabolism to regulate the proliferation, migration, and survival of endothelial cells which comprise the inner lining of blood vessels. Mitochondrial Complex III senses hypoxic conditions and generates mitochondrial reactive oxygen species which stabilize hypoxia-inducible factor (HIF-1 $\alpha$ ) protein. HIF-1 $\alpha$  induces the transcription of the *vegfa* gene, allowing the translation of vascular endothelial growth factor protein, which interacts with mature and precursor endothelial cells, mobilizing them to form new blood vessels. This cascade can be inhibited at specific points by means of gene knockdown, enzyme treatment, and introduction of naturally occurring small molecules, providing insight into the relationship between mitochondria and angiogenesis.



# WHAT ARE THE BENEFITS OF HYPOXIC TRAINING?

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Amplified pulmonary oxygen absorption

Boosted production of Erythropoietin Hormone (EPO) by the kidneys.  
Increased capillarization for greater oxygen delivery to the tissues, muscles and brain

Enhanced production and rejuvenation of mitochondria (the cell's hub for aerobic energy production) and mitochondrial enzymes, allowing more efficient use of oxygen for energy production and superior enzymatic anti-oxidative defense.

Decreased average Heart Rate and Blood Pressure

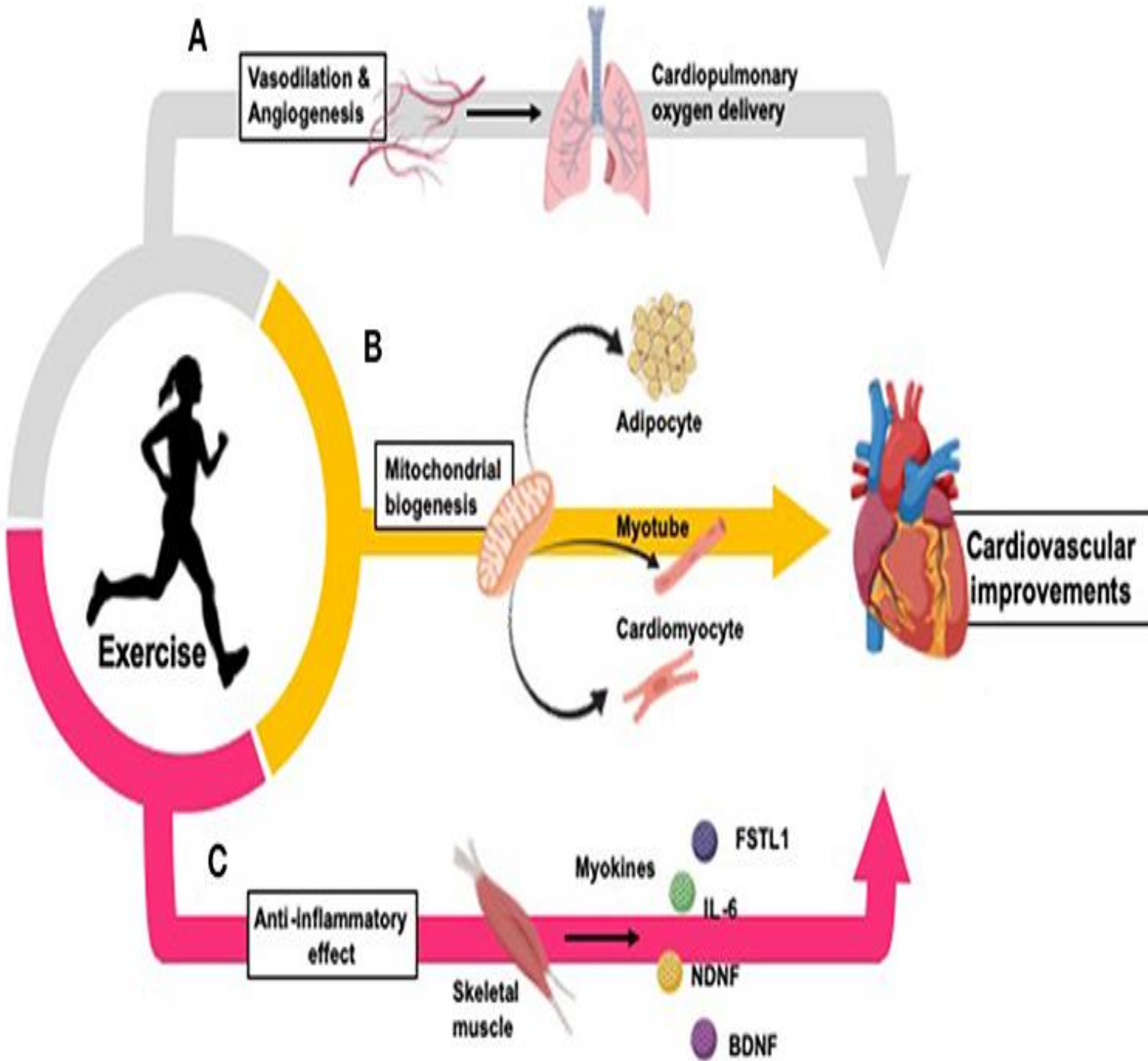
Increased production and release of Human Growth Hormone

Stimulation of fat metabolism

# LONG-TERM ADAPTATION IN AEROBIC AND RESISTANCE ACTIVITIES

## CARDIOVASCULAR

The most important adaptation for athletes is improved performance. Better performance is also an interest of exercise scientists because improving the capacity for exercise is important not only for athletes but also for everyone because improved aerobic fitness is related to a reduced risk of noncommunicable diseases such as heart disease, obesity, and diabetes.



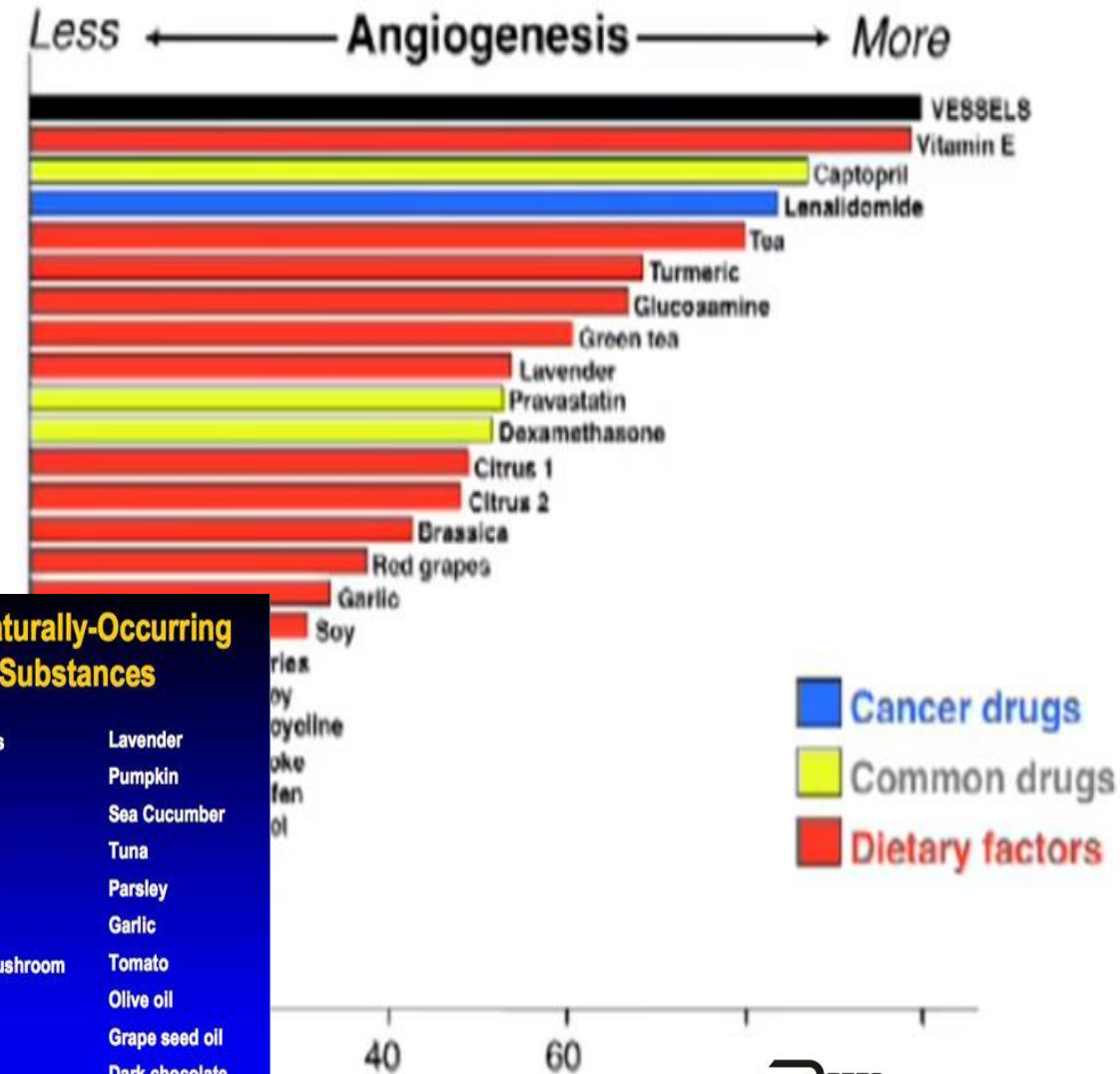


# DIETARY SOURCES OF NATURALLY-OCCURRING ANTIANGIOGENIC SUBSTANCES



**Dietary Sources of Naturally-Occurring Antiangiogenic Substances**

Green tea	Red grapes	Lavender
Strawberries	Red wine	Pumpkin
Blackberries	Bok choy	Sea Cucumber
Raspberries	Kale	Tuna
Blueberries	Soy beans	Parsley
Oranges	Ginseng	Garlic
Grapefruit	Maitake mushroom	Tomato
Lemons	Licorice	Olive oil
Apples	Turmeric	Grape seed oil
Pineapple	Nutmeg	Dark chocolate
Cherries	Artichokes	Others





# ANGIOGENESIS

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# THANK YOU

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