



**Regenerates human tissues and cells**

**HGF**

**(Hepatocyte growth factor)**

**and**

**Medicinal plant extract 『Ekc-1』**

**Institute of Oriental Medical Science Co., Ltd.**

**What is HGF ?**

# HGF

**H**epatocyte **G**rowth **F**actor

肝細胞増殖因子

Substances in our body

HGF was discovered from  
the phenomenon of liver regeneration.

HGF proliferates and regenerates  
hepatocytes.



**Among all organs within the human body, the liver has most amazing regenerative power.**



**Liver**

# Amazing liver regeneration



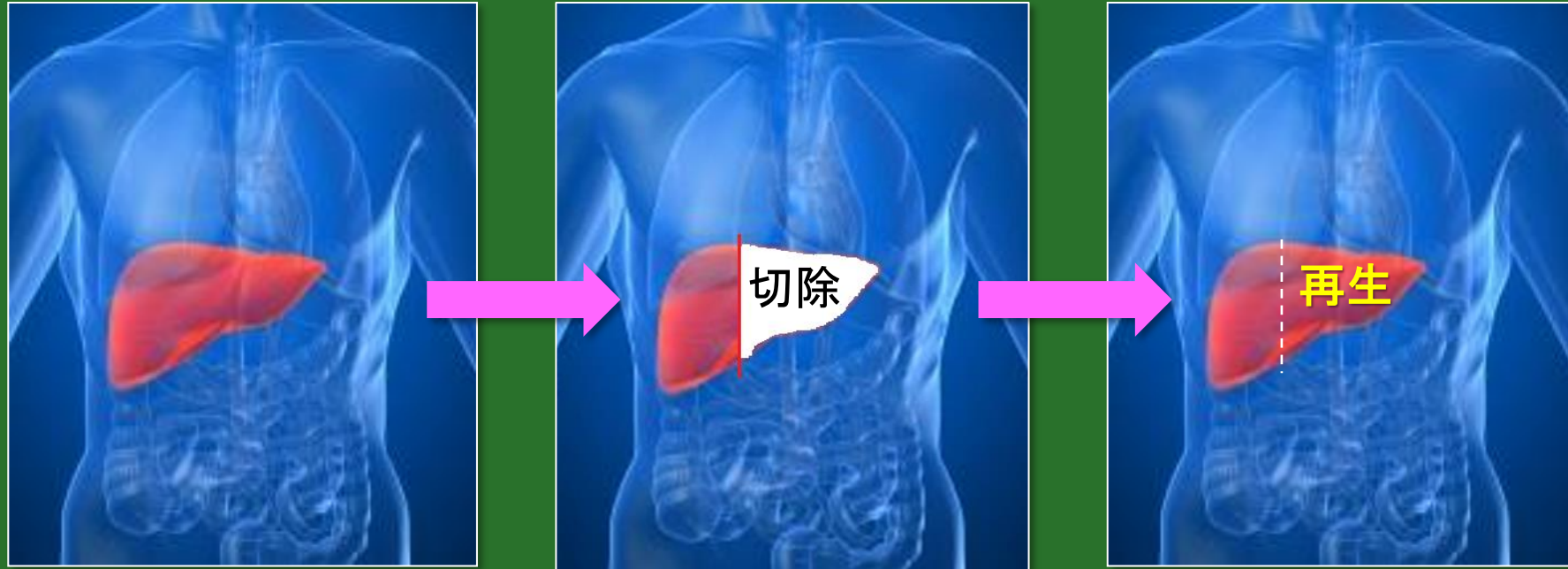
Liver resected in half



1 week later

The liver of a partially resected (1/2) rat is completely regenerated in 1 week

# Amazing liver regeneration



In the case of humans, it takes only one to several months to completely regenerate the original liver!!

**Liver with amazing regenerative power**



**The regenerative power of the liver has been known since the time of ancient Greek mythology.**

**Zeus, king of the Olympian gods, sentenced Prometheus to eternal torment for his transgression against him. The immortal Prometheus was bound to a rock, where each day an eagle, which was an emblem of Zeus, was sent to feed on his liver, which would then grow back overnight to be eaten again the next day.**

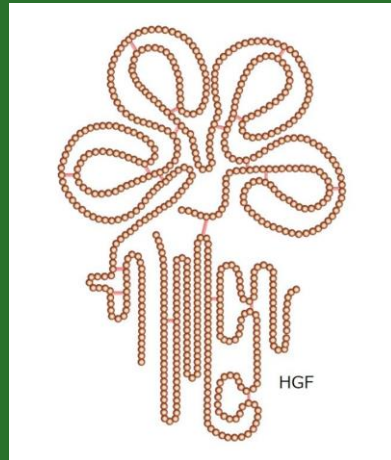




**In the past, researchers all over the world tried to discover the substance responsible for the high regenerative power of the liver, but could not elucidate it.**

**However, in 1984, this substance was finally found.**

Responsible was a protein with a special  
molecular structure



「 The protein proliferates  
hepatocytes and regulates  
cell growth, cell motility,  
and morphogenesis」

**H**epatocyte **G**rowth **F**actor



**H G F**

# Discoverer of HGF



中村敏一 Toshikazu Nakamura

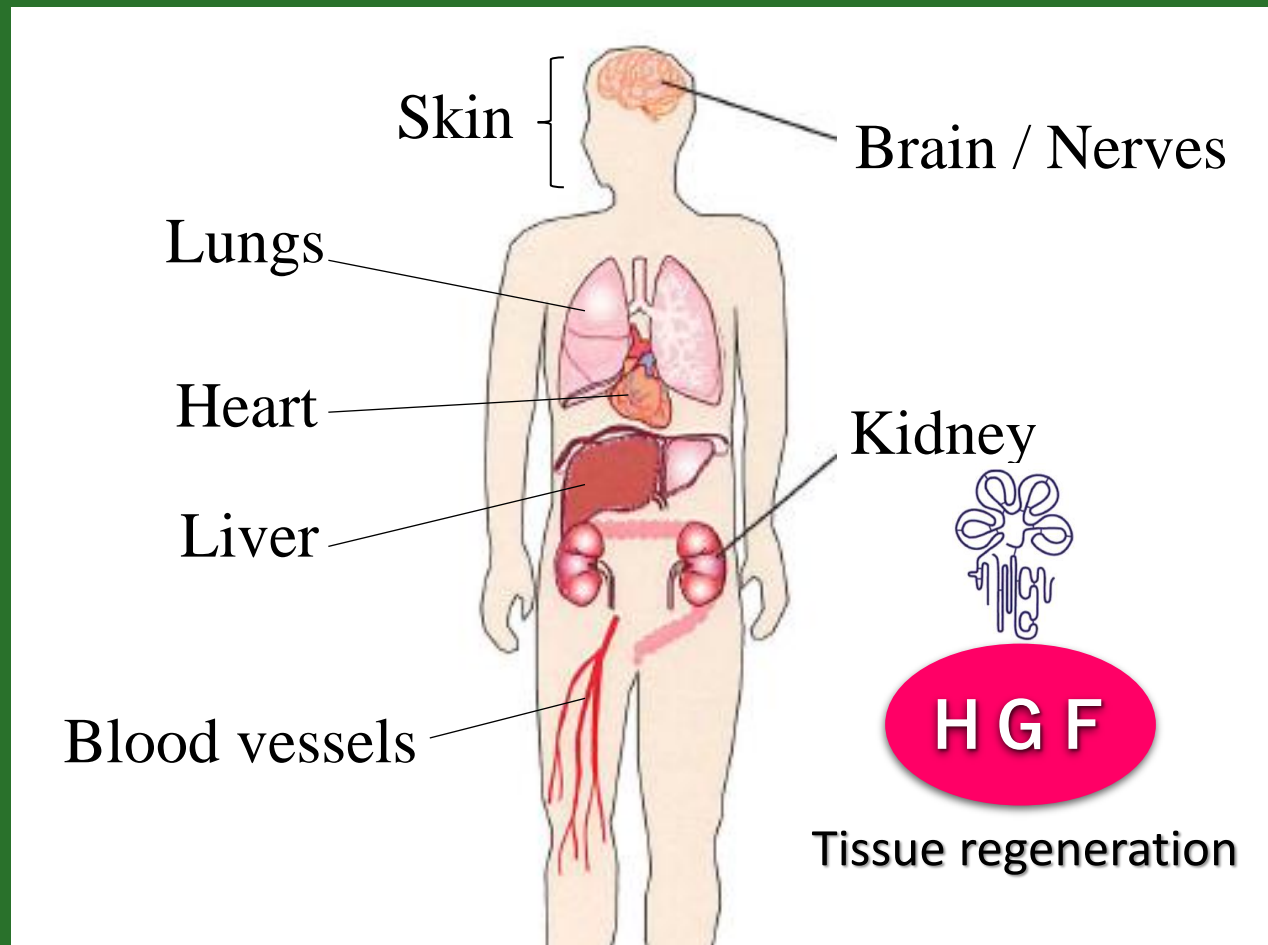
大阪大学先端科学イノベーションセンター  
再生創薬共同研究部門・特任教授、  
大阪大学名誉教授

He was nominated for **the Nobel Prize**  
for his work in separating and refining  
HGF for the first time in the world.



# Tissues and organs on which HGF is effective

HGF, which was discovered through research on the regenerative abilities of the liver, has been proven to work on various tissues and organs in subsequent studies, and is one of the leading candidates for regenerative medicine.



# Regenerative medicine research on HGF

Drug discovery venture  
business from Osaka University  
School of Medicine

Founded by Professor Toshikazu Nakamura  
while being in office at Osaka University



## AnGes, Inc.

※HGF Gene drug discovery



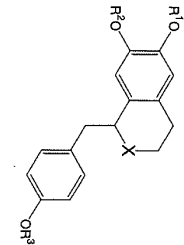
## Kringle Pharma

※Synthetic HGF protein drug discovery



## Neurogen

※In vivo HGF production inducing  
drug discovery



## アンジェス、遺伝子治療薬に承認 足の血管再生

2019/3/26 19:11

保存 共有 印刷 共有 ツイート その他

大阪大学発ベンチャーのアンジェスは26日、開発を進めていた体内に遺伝子を入れて病気を治す「遺伝子治療薬」が厚生労働省から承認を受けたと発表した。対象は重症の動脈硬化による足の血管狭窄症。患者は約1000人。承認は国内初。

AnGes developed an HGF gene drug that regenerates blood vessels in the legs and has been approved by the government.

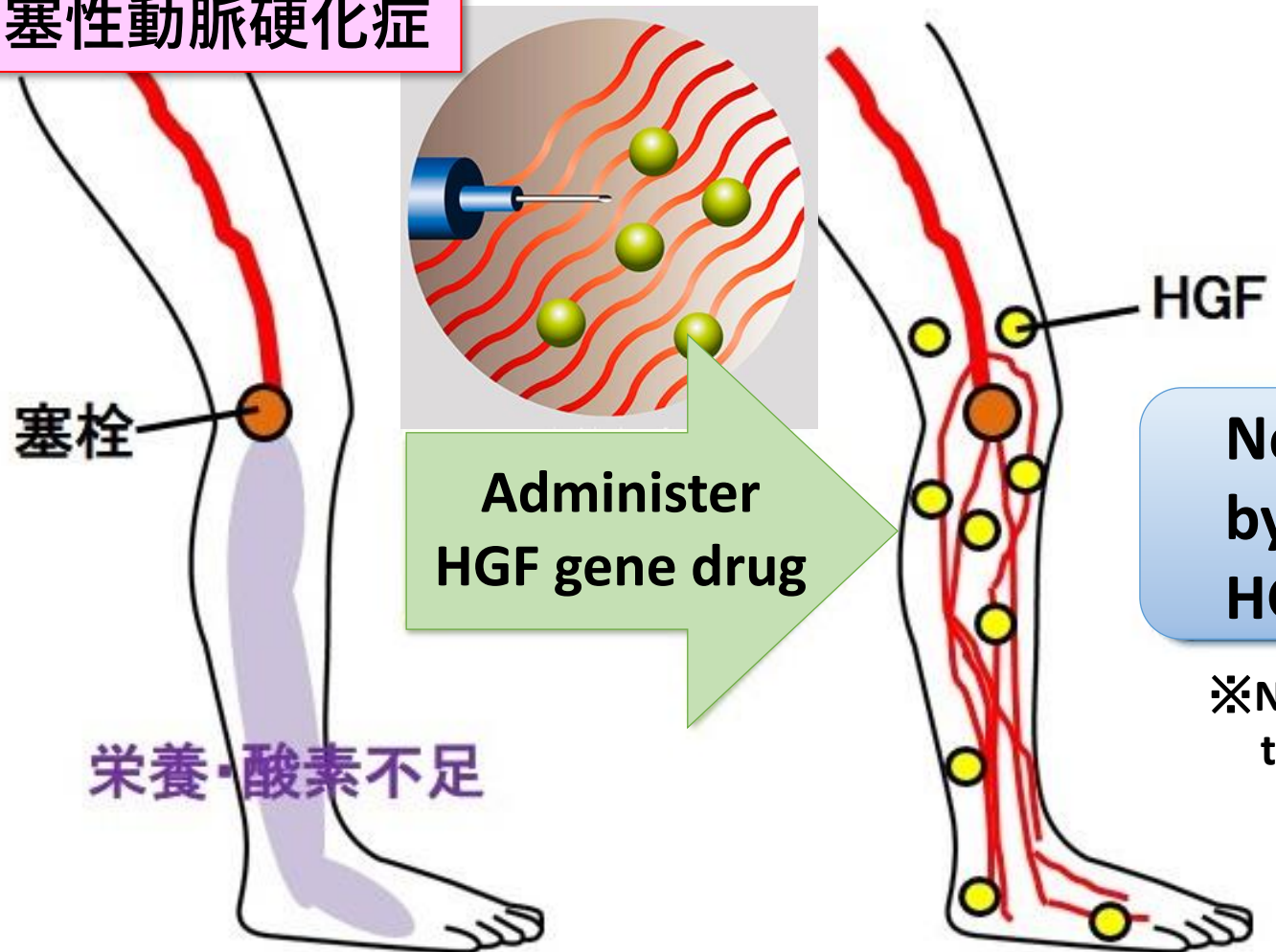
遺伝子を注射して治療する。十分な知識と経験を持つ医師や施設の使用、販売後の薬効



# 重症虚血肢

## 閉塞性動脈硬化症

新薬情報オンライン



**New blood vessels are regenerated by the action of HGF produced by HGF gene drug.**

※New blood vessels are regenerated by bypassing the occluded part.

リリース先：宮城県政記者会、文部科学省記者クラブ、科学記者会、大阪科学・大学記者クラブ



東北大学



大阪大学



CRIETO



2016年5月13日

報道機関 各位

東北大学病院

東北大学病院臨床研究推進センター

東北大学大学院医学系研究科

大阪大学医学部附属病院

大阪大学大学院医学系研究科

筋萎縮性側索硬化症（ALS）を対象とした肝細胞増殖因子（HGF）の

第Ⅱ相試験（医師主導治験）を開始

**HGF clinical trials for ALS are being conducted  
at Osaka University and Tohoku University.**



# 脊髄損傷の薬 治験へ

## 慶大リハビリ以外の第一歩

慶大は16日、脊髄損傷の新しい治療薬の臨床試験（治験）を6月中にも始めると発表した。細胞の再生を促す働きがあるHGF

（肝細胞増殖因子）というたんばく質から作った薬を使う。HGFによる脊髄損傷の治験は国内初という。同大によると、新たに脊

### 慶大など 脊髄損傷に新治療

### 肝細胞増殖因子を注射

事故などで脊髄を損傷してから78時間以内に、神経を保護するたんばく質を投与し、機能回復を目指す新薬の臨床試験（治験）を始めると、岡野栄之・慶大教授（再生医学）とベンチャー企業「クリンケルファーマ」（大阪府）のチームが16日発表した。国内で年間約5000人の新規患者の約8割で症状の改善を期待できるという、安全性を確かめる。治験は月内に国内2カ所の病院で実施し、2016年10月まで続ける。対象は、重度の急性期患者48人。患者の同意を得て、2班に分けて神経細胞を保護する機能を持った「肝細胞増殖因子（HGF）」が疑似薬を腰から注射する。1週間ごとに計5回投与し、機能回復の効果を比較する。

脊髄損傷は外傷による損傷に加え、生き残った神経細胞も炎症で死滅し、運動機能や感覚がまひする。有効な治療薬はない。HGFは炎症を抑制したり、神経や血管の再生を促したりする効果がある。チームは、ラットやサルの中間マウスセットの実験では、正常の

患者は日本で。交通事故やなどが原因となり以外に有効く、薬による

れている。

のは、同大の教授（整形外）は、傷を負った重たい患者

機能が回復した。

累積患者数は上。慶大の中（整形外科）

経が切れてい

者の生活の質

期的な治療法

した。今後、

を対象に人工

（iPS細胞）

幹細胞の移植

る。

使った治験で

慶大が、筋萎

症（ALS）

ている。脊髄

札幌医科大学が今

自から採取した

し、神経を再

を始めた。

【千葉紀和】

HGF clinical trials for Spinal Cord Injury are being conducted at Keio University.





# おおさか地域創造ファンド

Active Osaka Promotion Fund

医薬品・医療機器・iPS細胞(再生医療・創薬等)事業化・成長促進支援プロジェクト

## ◆薬草類に含まれるHGF誘導因子を活用した 認知症予防・治療薬の開発・導出事業

株式会社漢方医科学研究所／株式会社ニューロゲン

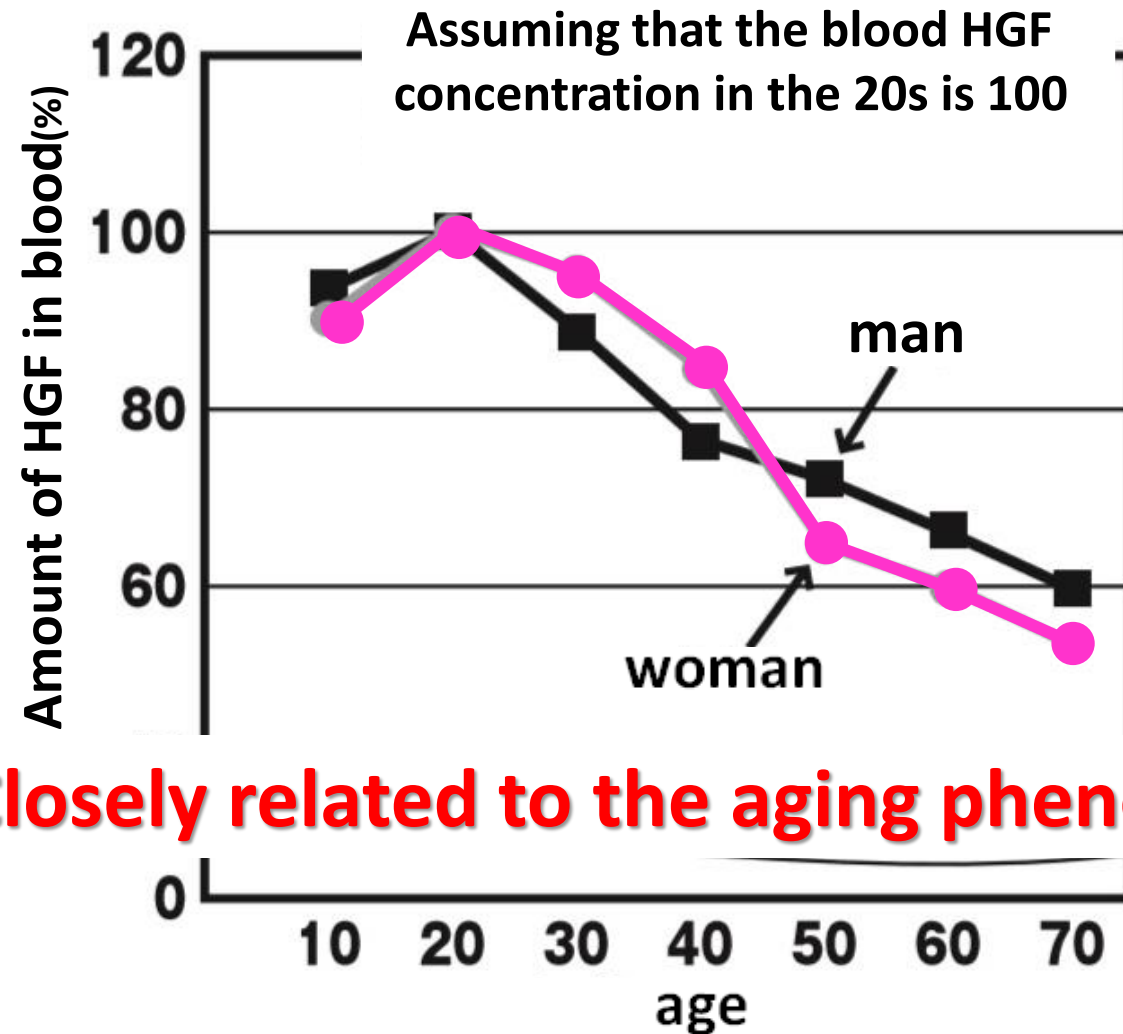
代表企業：株式会社漢方医科学研究所  
大阪市北区西天満 1 丁目 7 - 2 0



Development of therapeutic agents for dementia utilizing HGF production-inducing factors contained in medicinal plants.

**HGF is a substance (protein)  
that exists in our body**

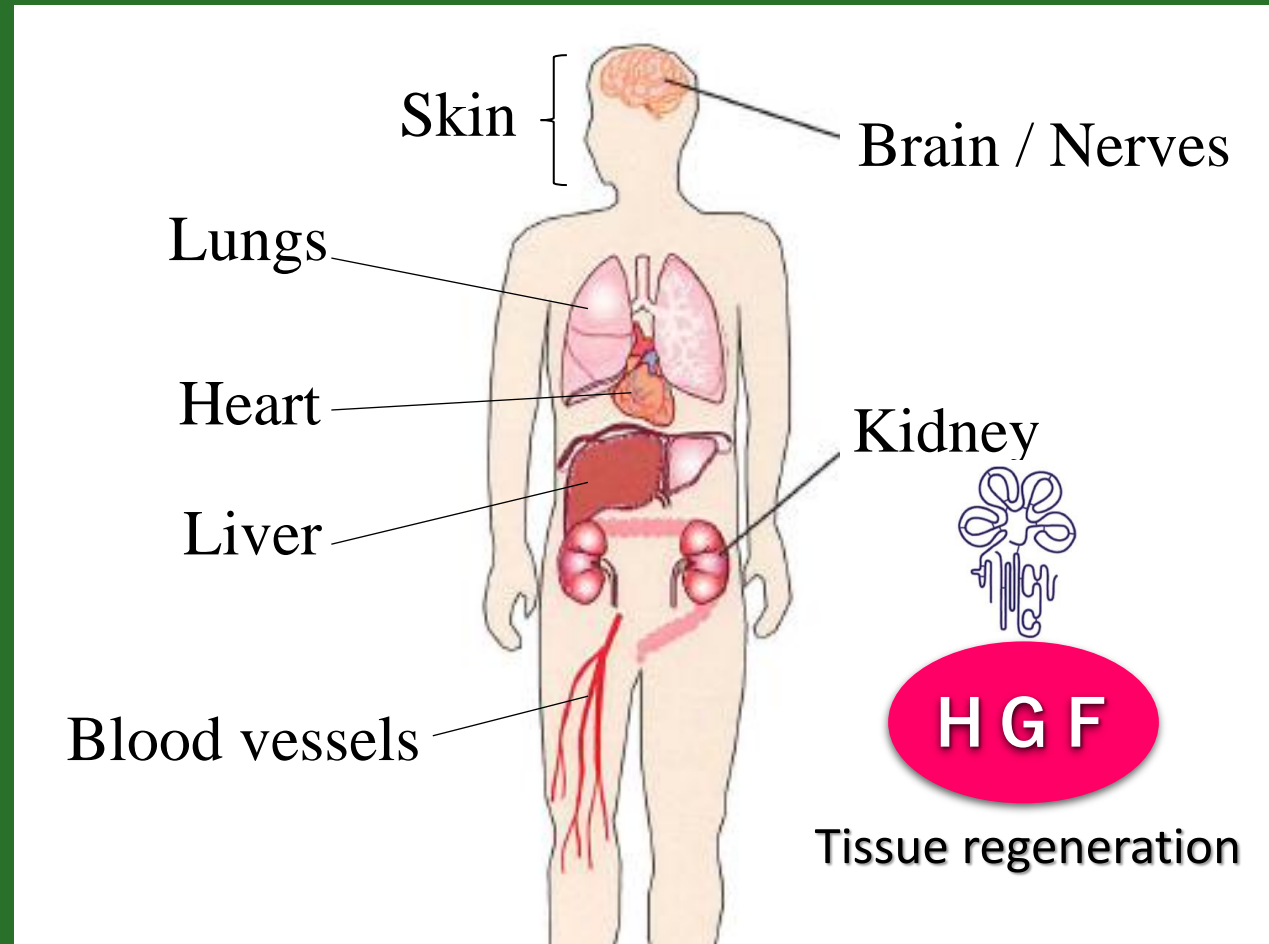
# HGF concentration in blood that decreases with age



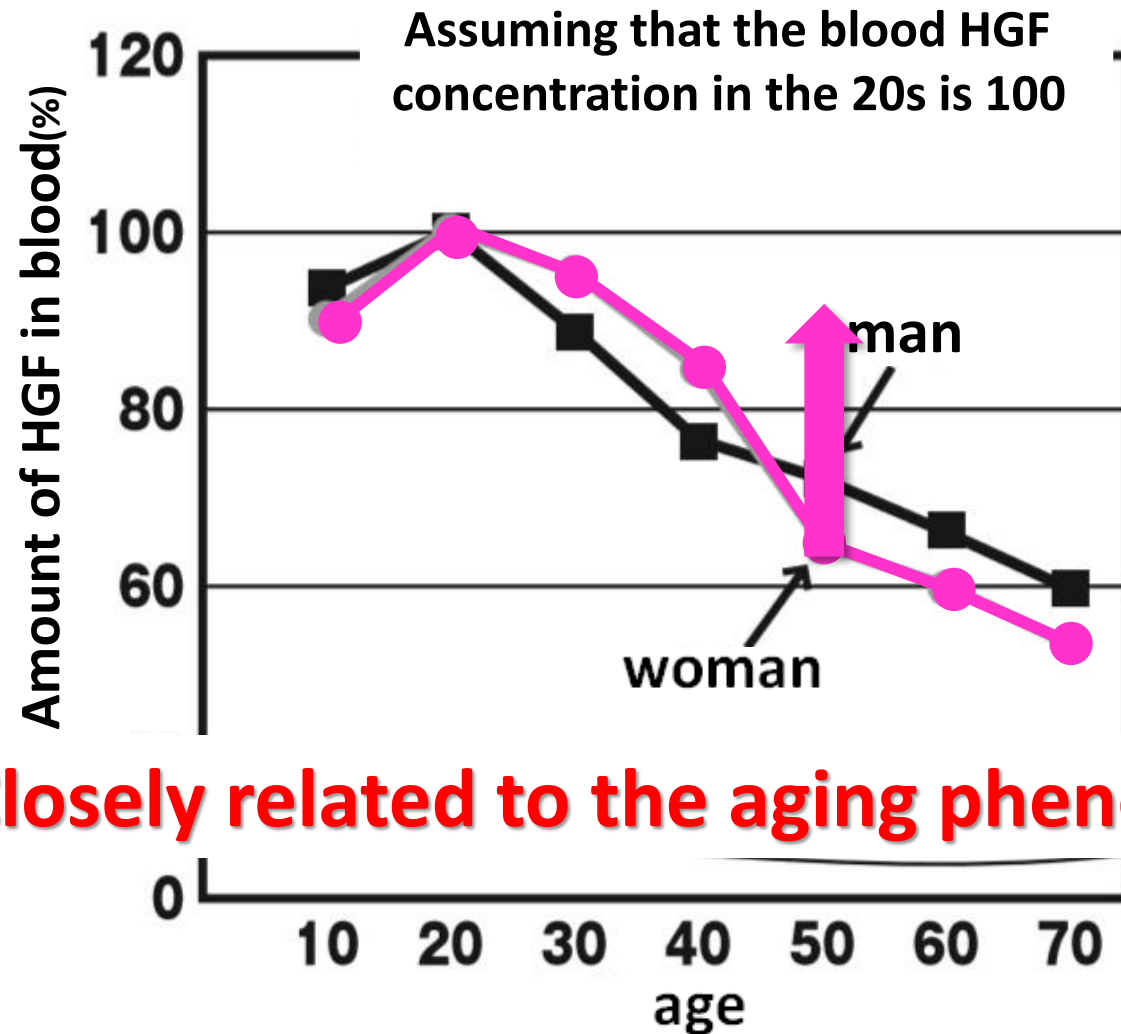
**Closely related to the aging phenomenon**



# Tissue and organ functions that decline with age



# HGF concentration in blood that decreases with age

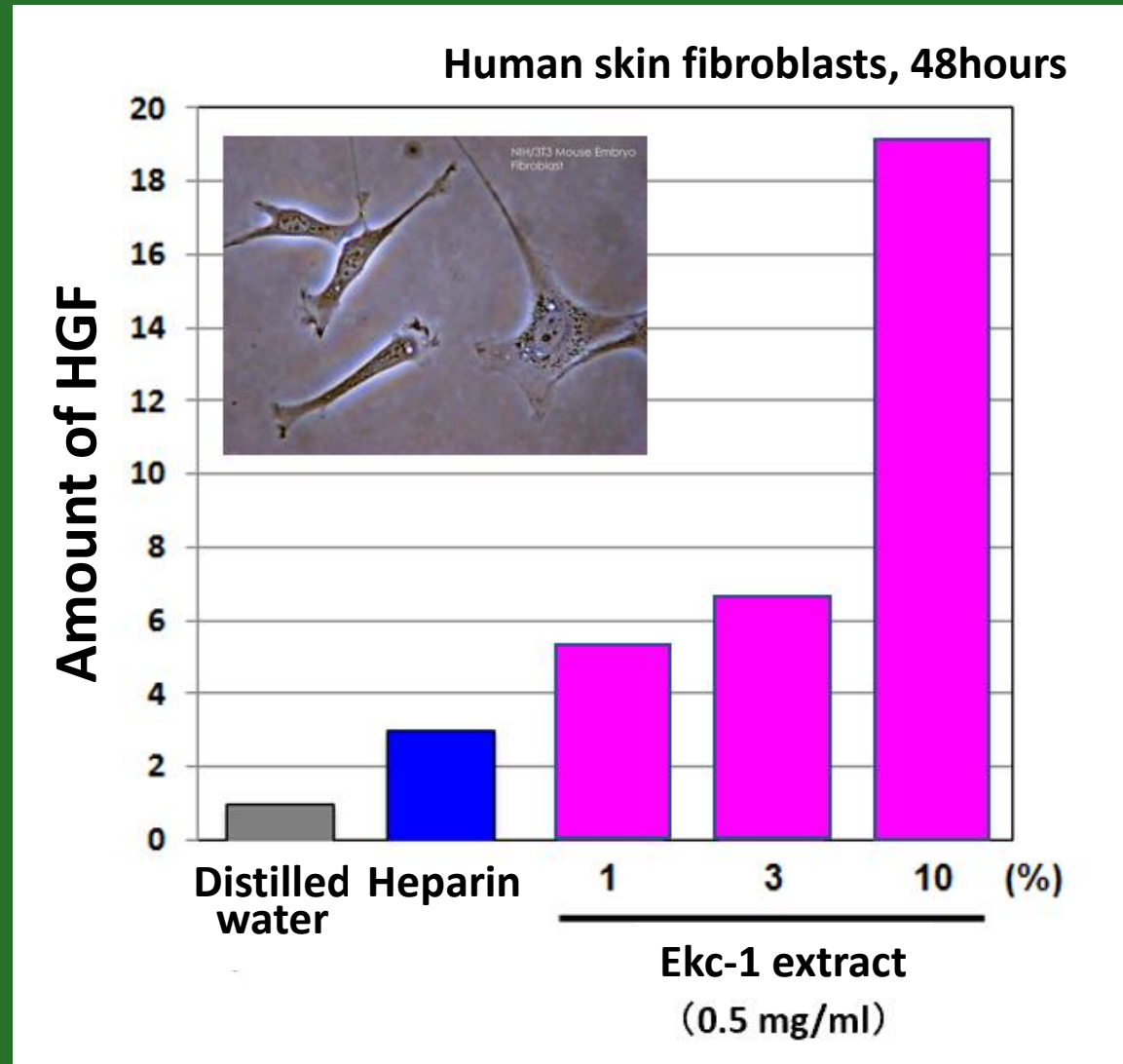


**Closely related to the aging phenomenon**

# Developed "Ekc-1", plants extract that induces high-level production of HGF



# HGF production-inducing activity of "Ekc-1"





## Gagome kelp fucoidan's tissue regeneration promoting action



研究論文・学会発表 ▶

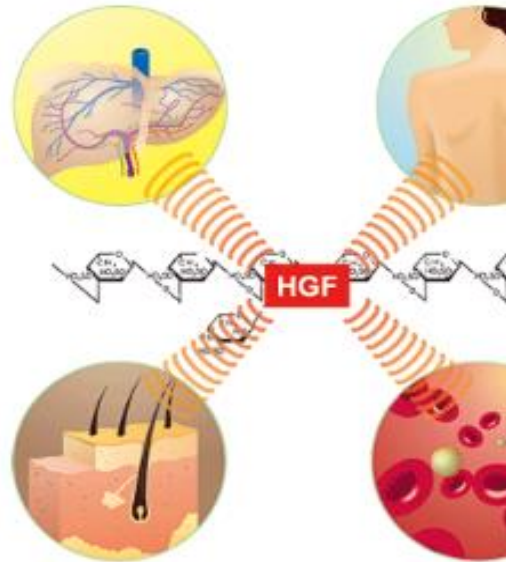
- 1 抗腫瘍作用 ▶
- 「きのこテルペン」との併用作用 ▶
- 高分子量の重要性 ▶
- 2 ヒトの免疫機能に対する有効性 **NEW**
- 3 乳酸菌との併用効果
- 4 インフルエンザ感染予防作用 ▶
- 5 抗血栓作用 ▶
- 6 組織再生促進作用
- 7 ヘリコバクターピロリ、感染抑制作用 ▶
- 8 アレルギー抑制作用 ▶

### ガゴメ昆布「フコイダン」の組織再生促進作用

ガゴメ昆布「フコイダン」の摂取により、肝臓をはじめ様々な組織の再生に効果が期待できます。

肝細胞増殖因子(HGF)は肝細胞に対する強い増殖促進作用を持つタンパク質です。最近では、腎臓、肺、血管、皮膚など多くの組織や器官の再生因子であることが明らかになってきており、肝炎の治癒促進作用、育毛作用、抗がん剤による血小板の減少を抑制する作用など、傷ついた様々な器官・組織・細胞の再生を促進する作用が知られてきています。

タカラバイオでは、ガゴメ昆布「フコイダン」のひとつである「F-フコイダン」からHGFを産生を促す作用があることを解明しました。



## フコイダン<エキス>400

1袋当りガゴメ昆布「フコイダン」  
**400mg**



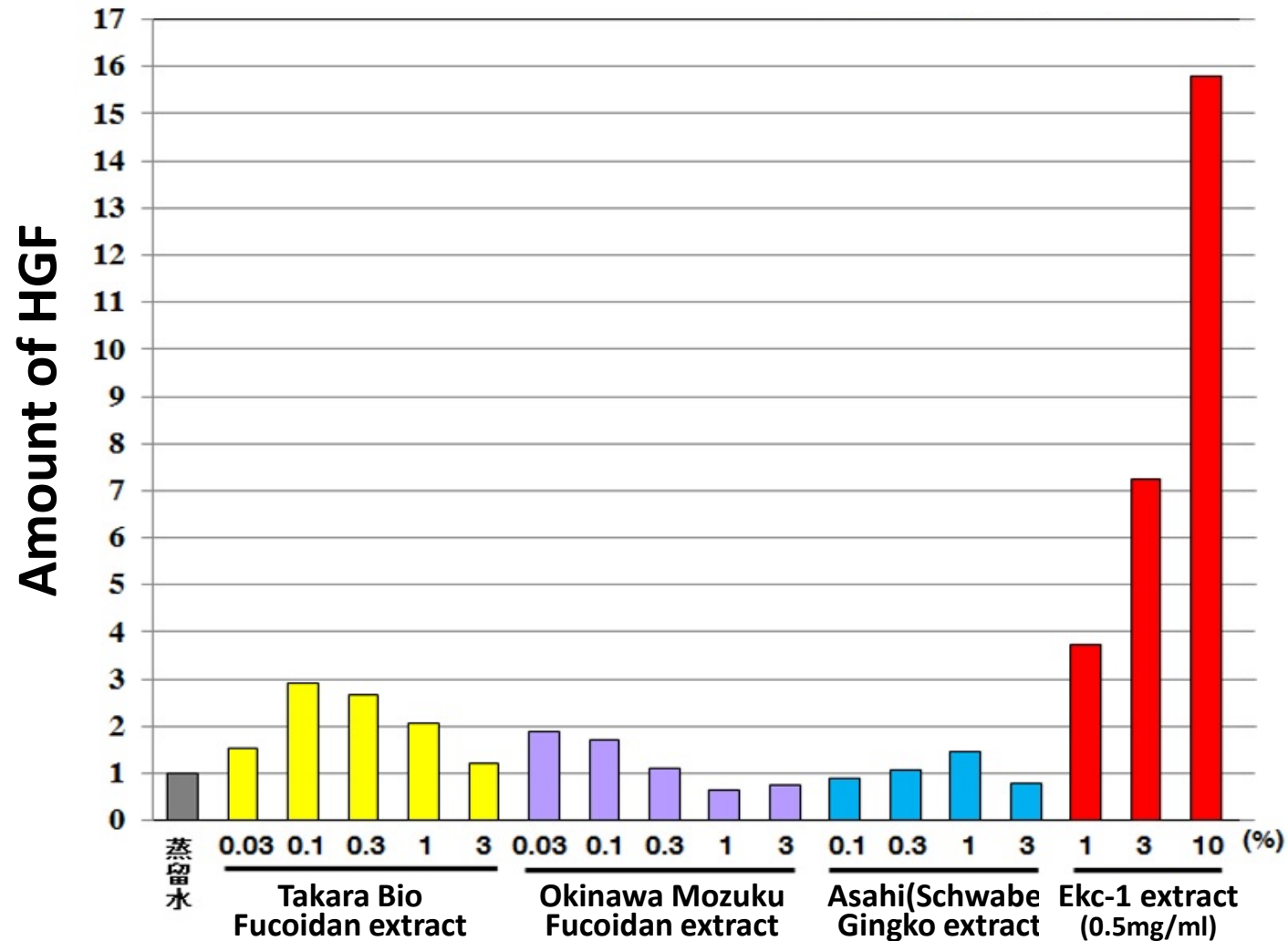
- ・1袋当りガゴメ昆布「フコイダン」400mg配合
- ・北海道産ガゴメ昆布使用
- ・飲みやすい紅茶風味
- ・保存料、着色料不使用

1日1袋目安(30日分)  
1箱30袋入り

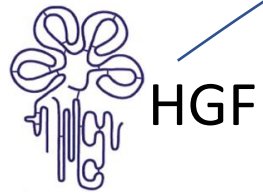
通常価格 **29,160円** (税込)

送料  
無料

# Comparison with HGF production-inducing activity of other products



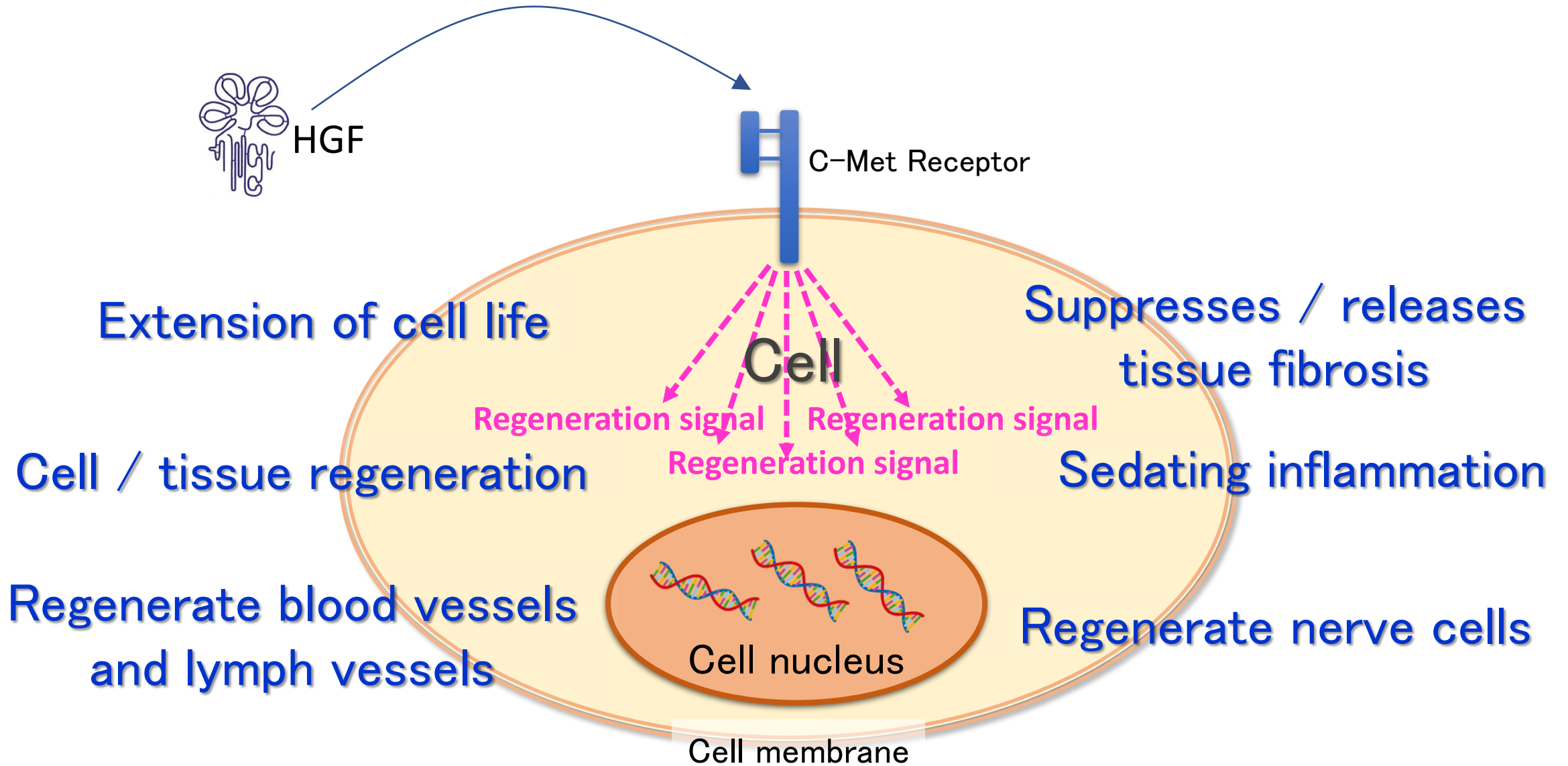
**How does HGF work?**



HGF



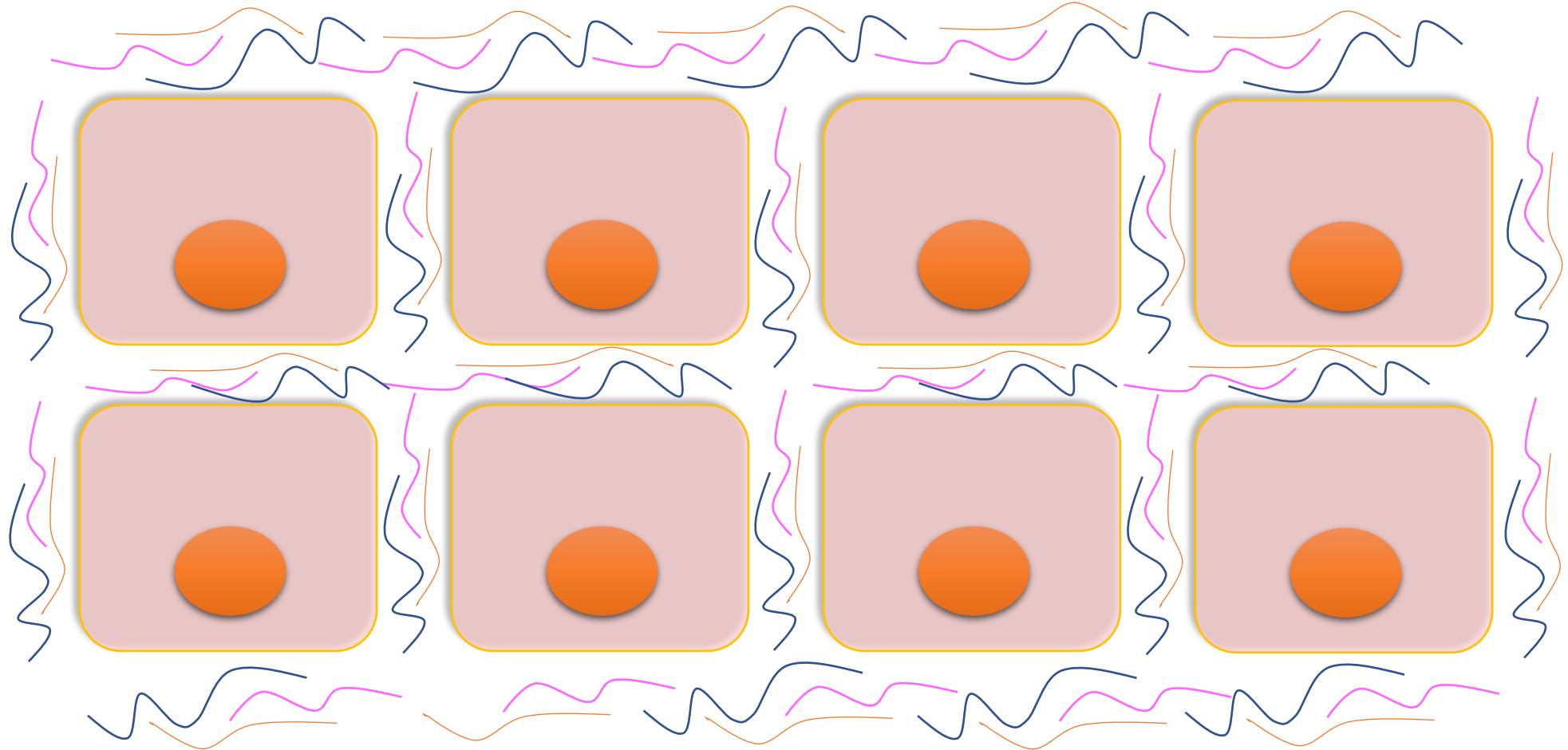
C-Met Receptor



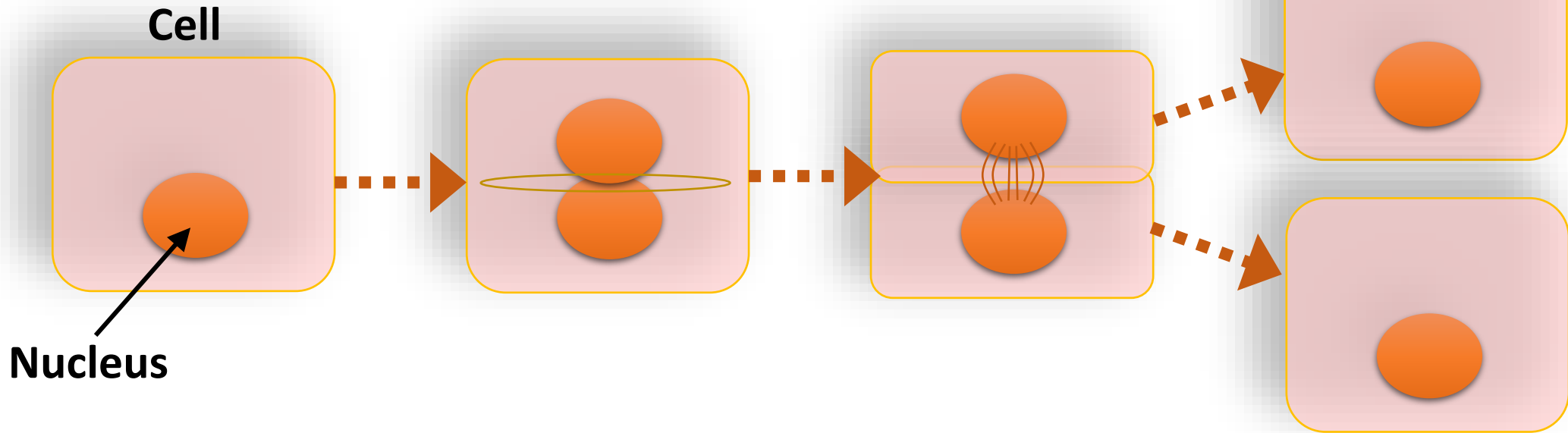


# Fibrosis of tissue (aggregate of cells)

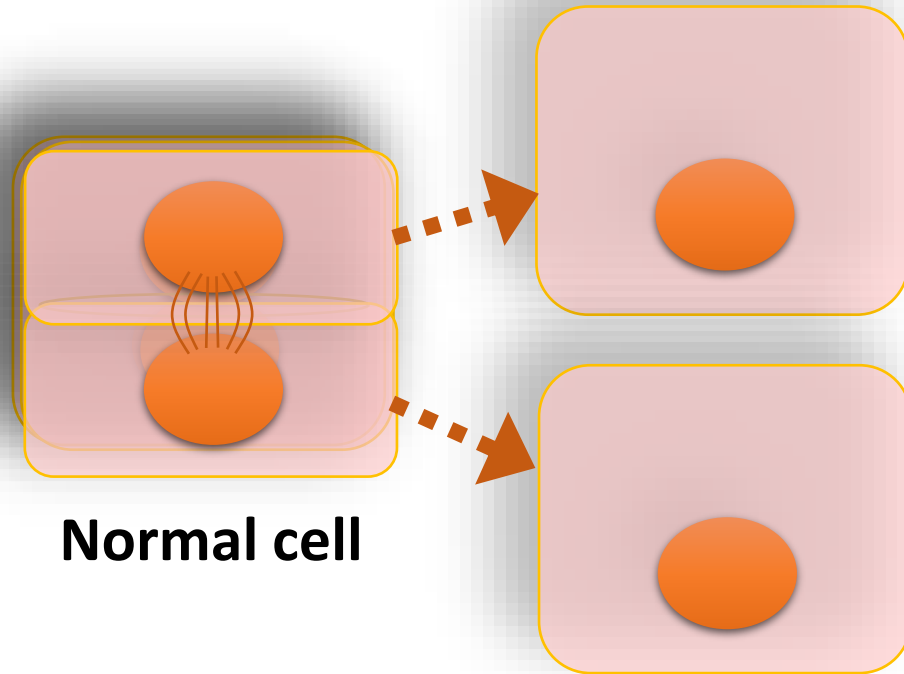
**Protein fibers such as collagen, elastin, proteoglycan, fibronectin, etc.**



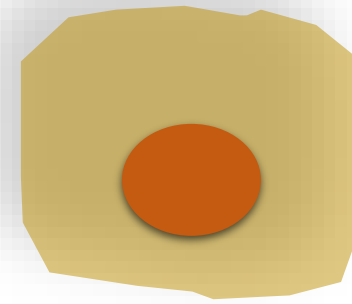
# Cells constantly divide and proliferate and are replaced by new cells



# Cells constantly divide and proliferate and are replaced by new cells

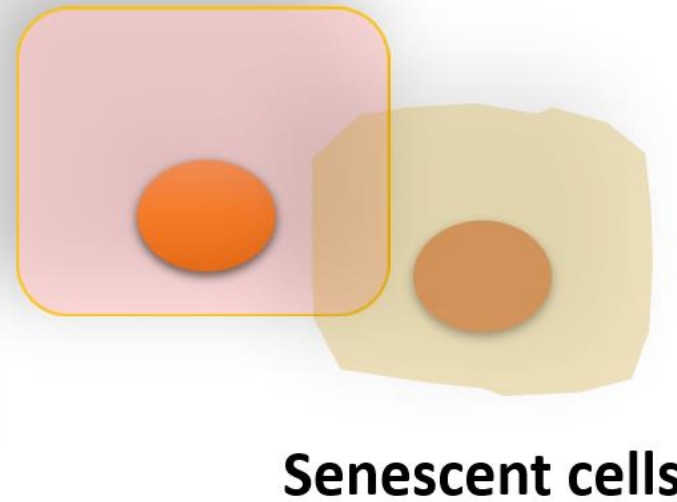
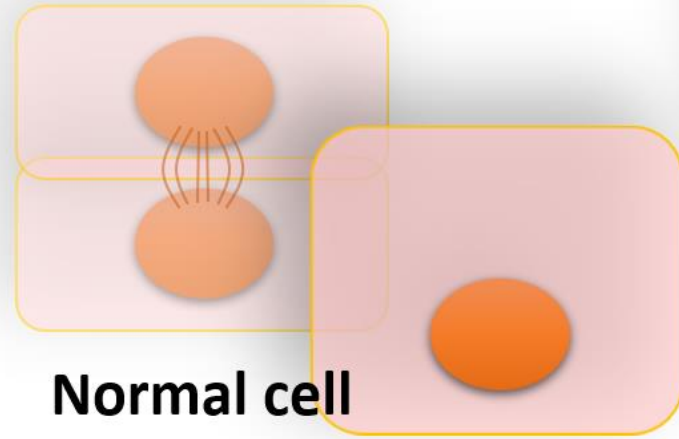


**Normal cell**



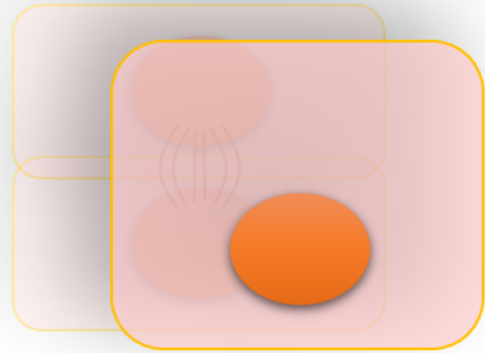
**Normal cell**

# Cells constantly divide and proliferate and are replaced by new cells





# Cells constantly divide and proliferate and are replaced by new cells

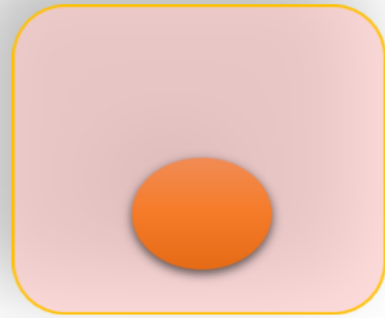


**Normal cell**

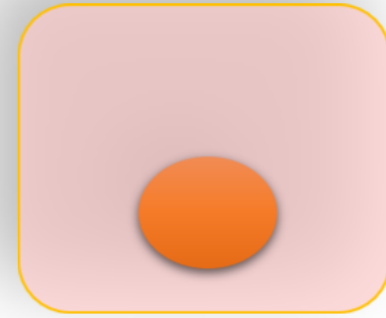


**Senescent cells**

# Cells constantly divide and proliferate and are replaced by new cells



**Normal cell**

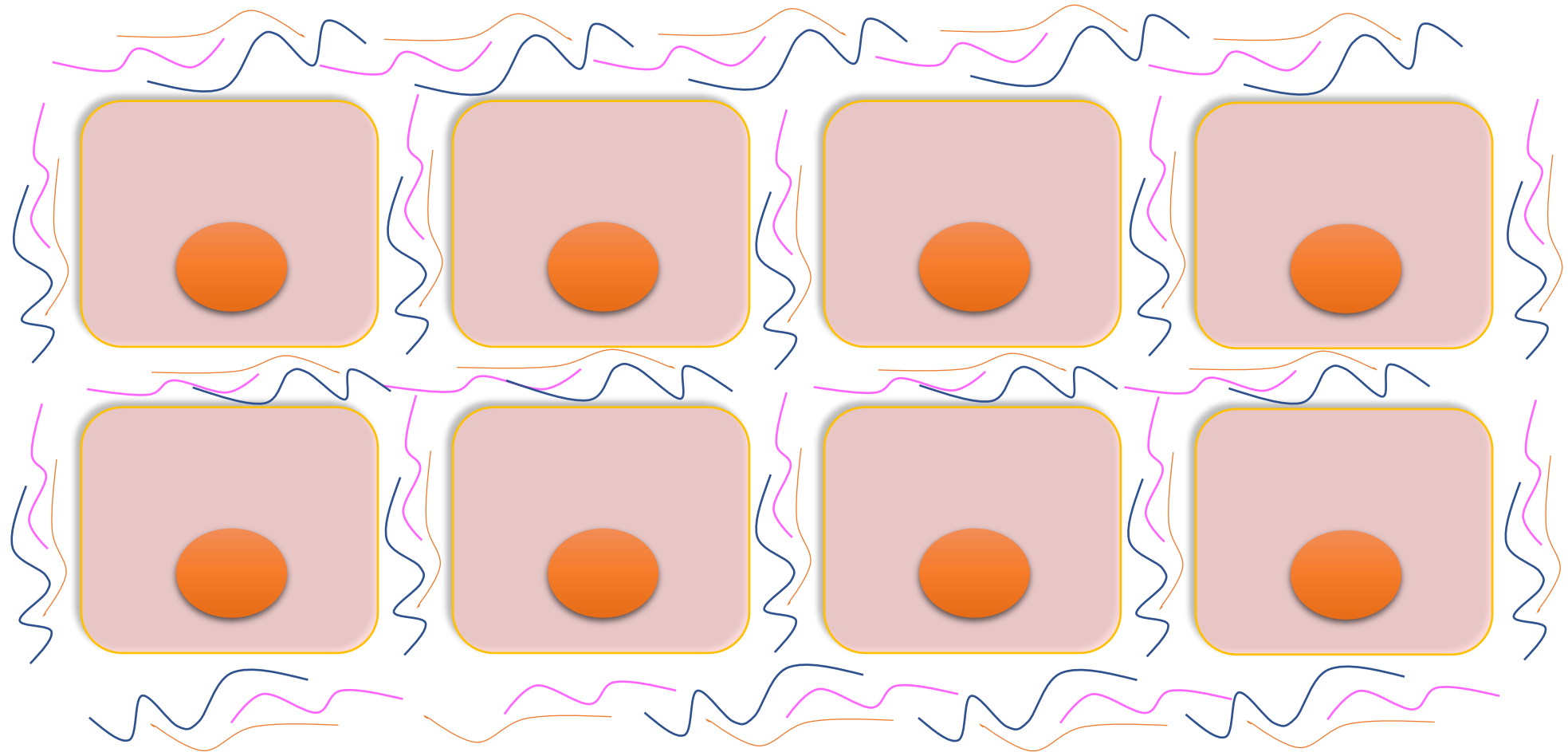


**Normal cell**

# Cells constantly divide and proliferate and are replaced by new cells

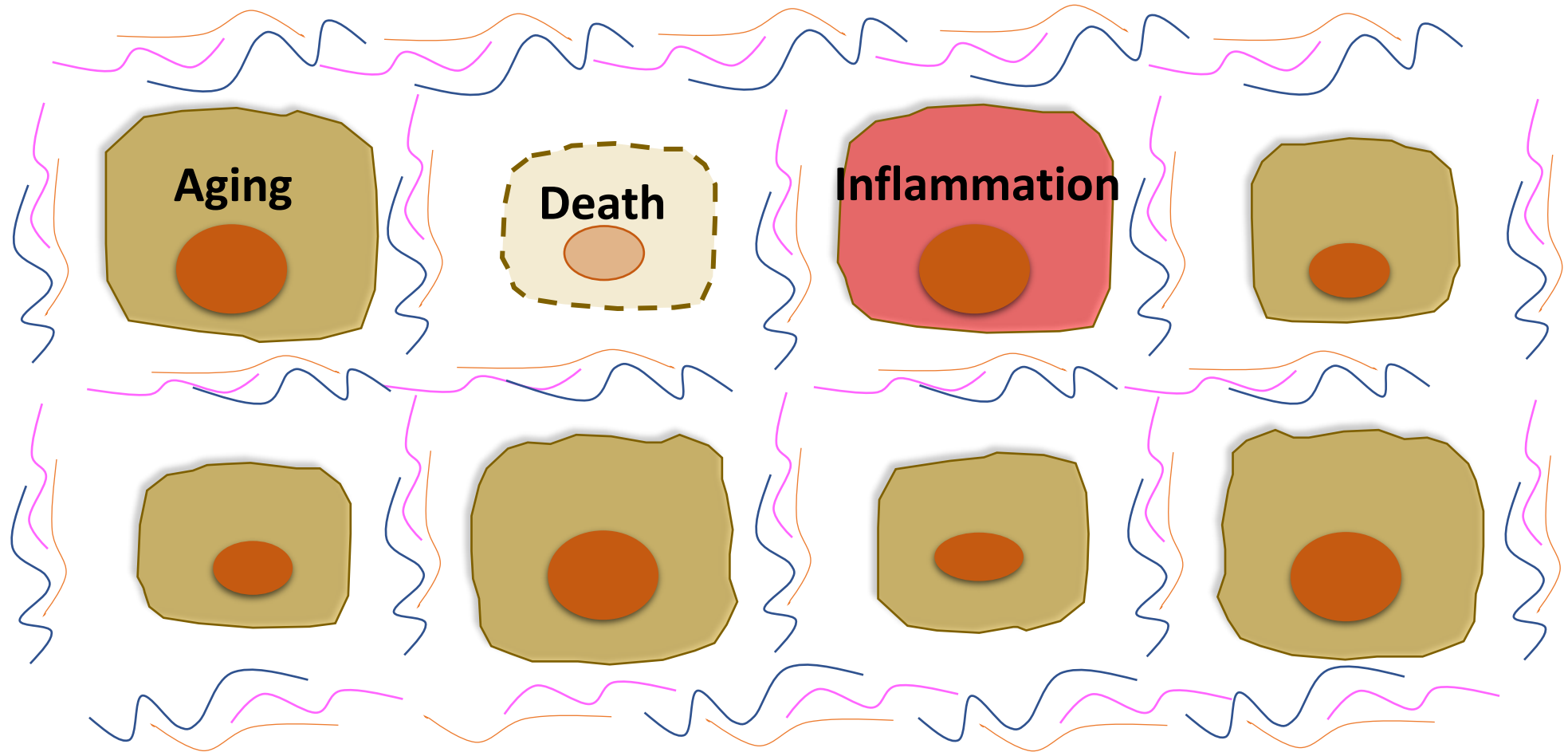
- Gastric mucosa 3 ~ 5 day
- Intestinal mucosa 1 ~ 3 day
- Liver 1 month ~ 1 year
- Kidney 1 month ~ 1 year
- Bone 2 ~ 3 year
- Blood 3 ~ 4 month
- Skin 28 day ?

# Fibrosis of tissue (aggregate of cells)

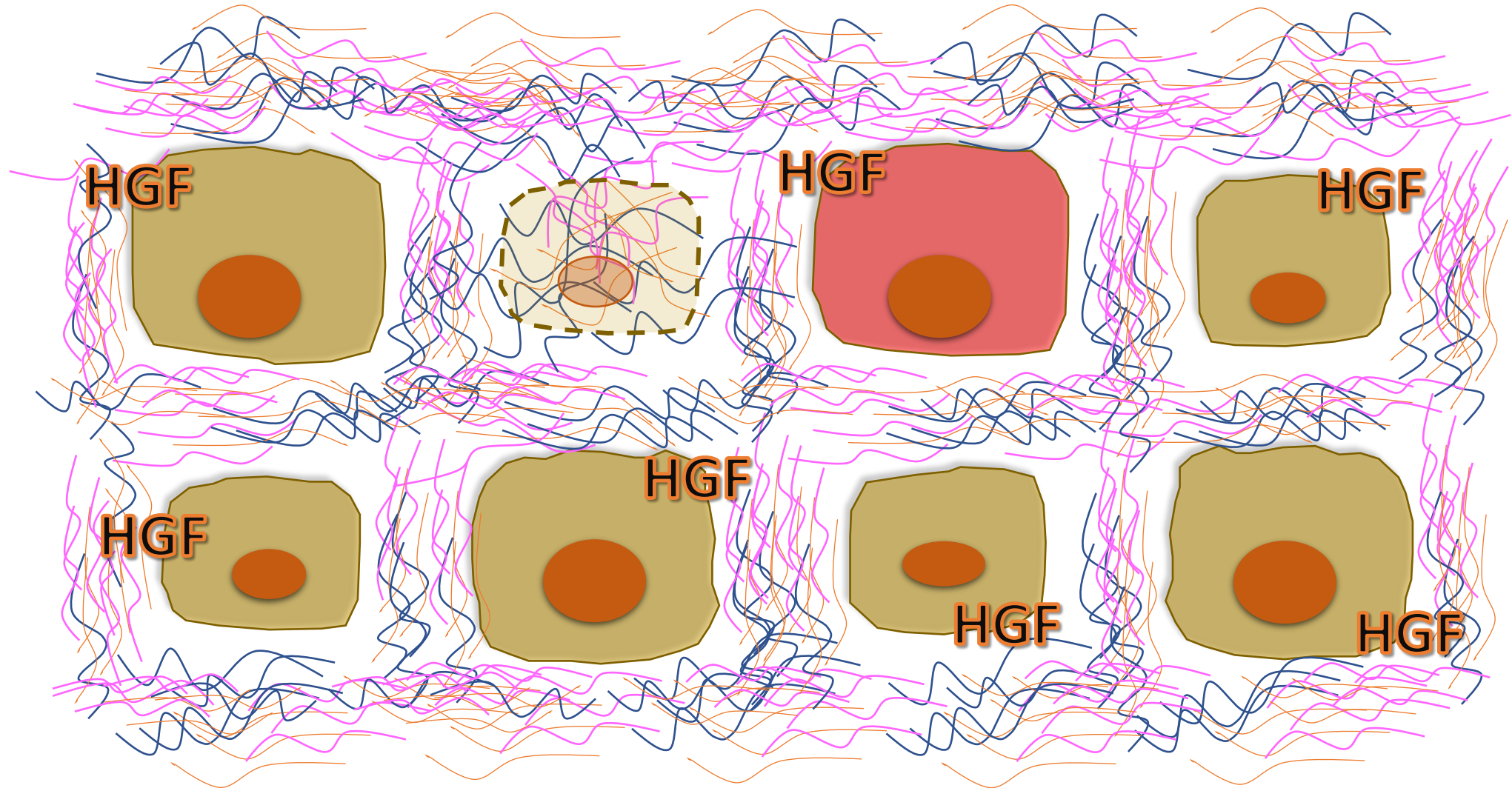




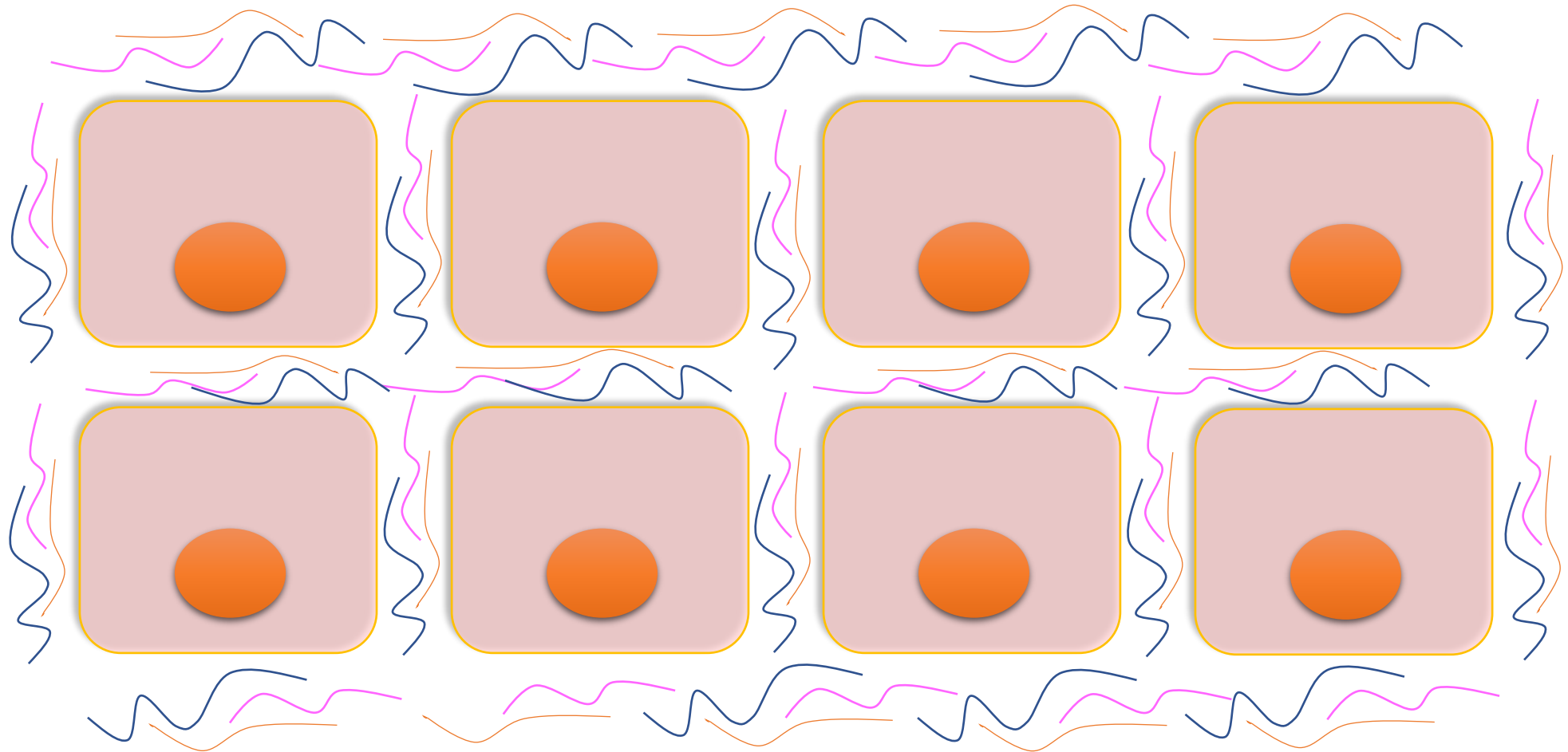
# Fibrosis of tissue (aggregate of cells)



# Fibrosis of tissue (aggregate of cells)

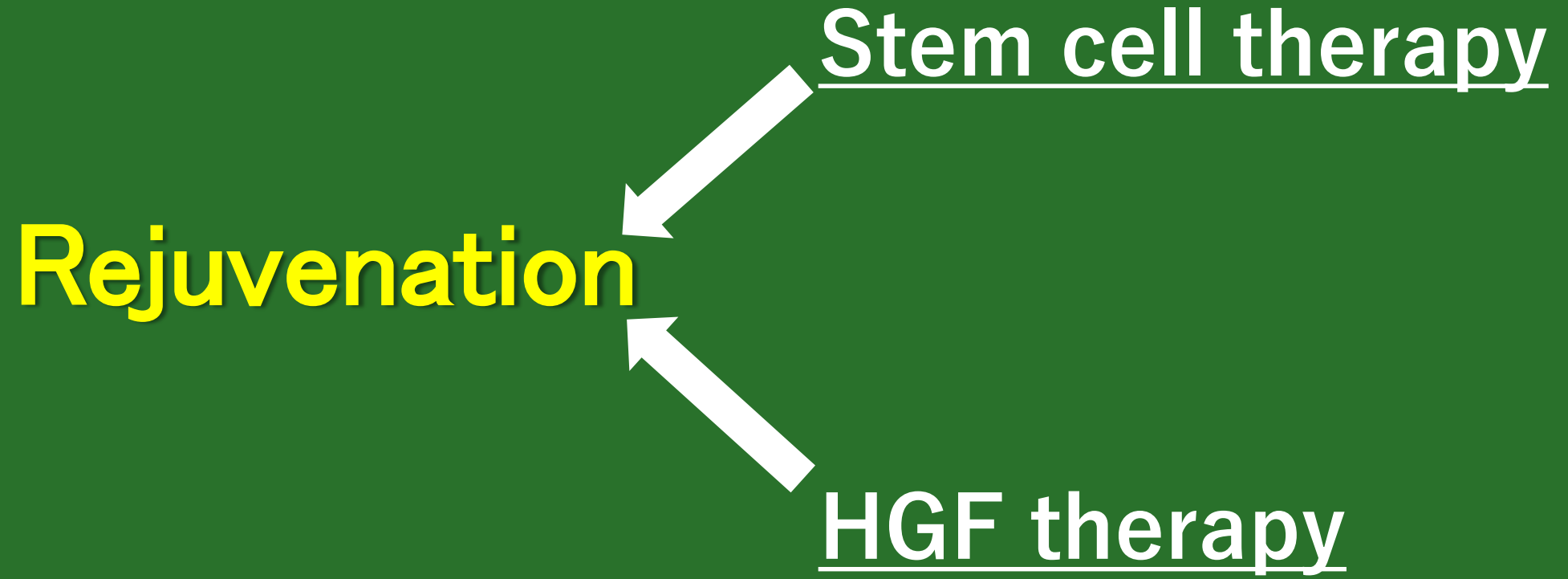


# HGF regenerates cells and improves tissue fibrosis



**This is  
the rejuvenation of cells (tissues)**





# Stem cell therapy

**Brain**  
**Spinal cord**

Cerebral hemorrhage  
Cerebral infarction  
Alzheimer's disease  
Spinal cord injury

**Heart**

Myocardial infarction

**Lung**

COPD  
Interstitial pneumonia

**Liver**

Hepatitis, Cirrhosis

**Kidney**

Chronic renal dysfunction



blood vessels  
rejuvenation

Skin  
rejuvenation

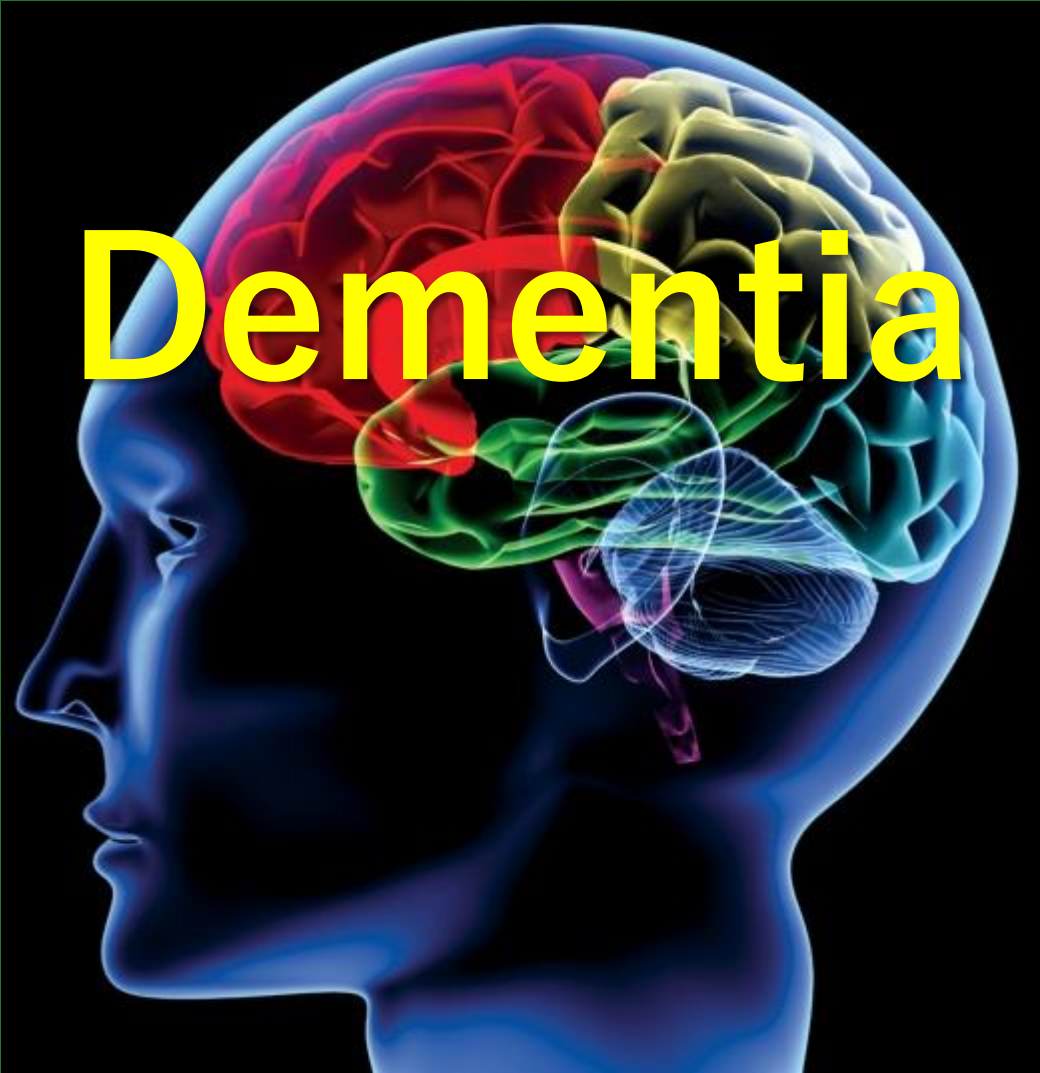
Joint  
rejuvenation

Diabetes mellitus

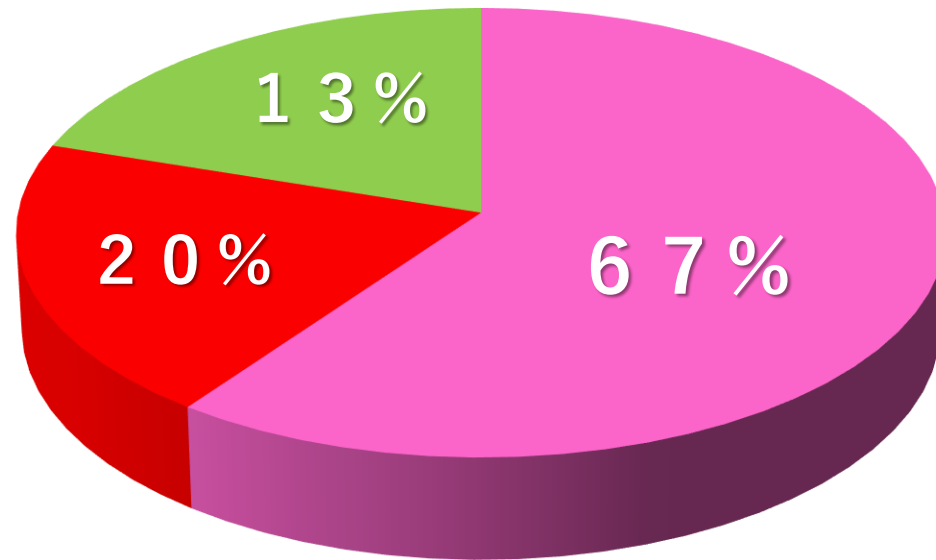
Aging symptoms

**Stem cell therapy and HGF therapy  
have almost the same effect.**

# Aging of brain cells



# Type of dementia

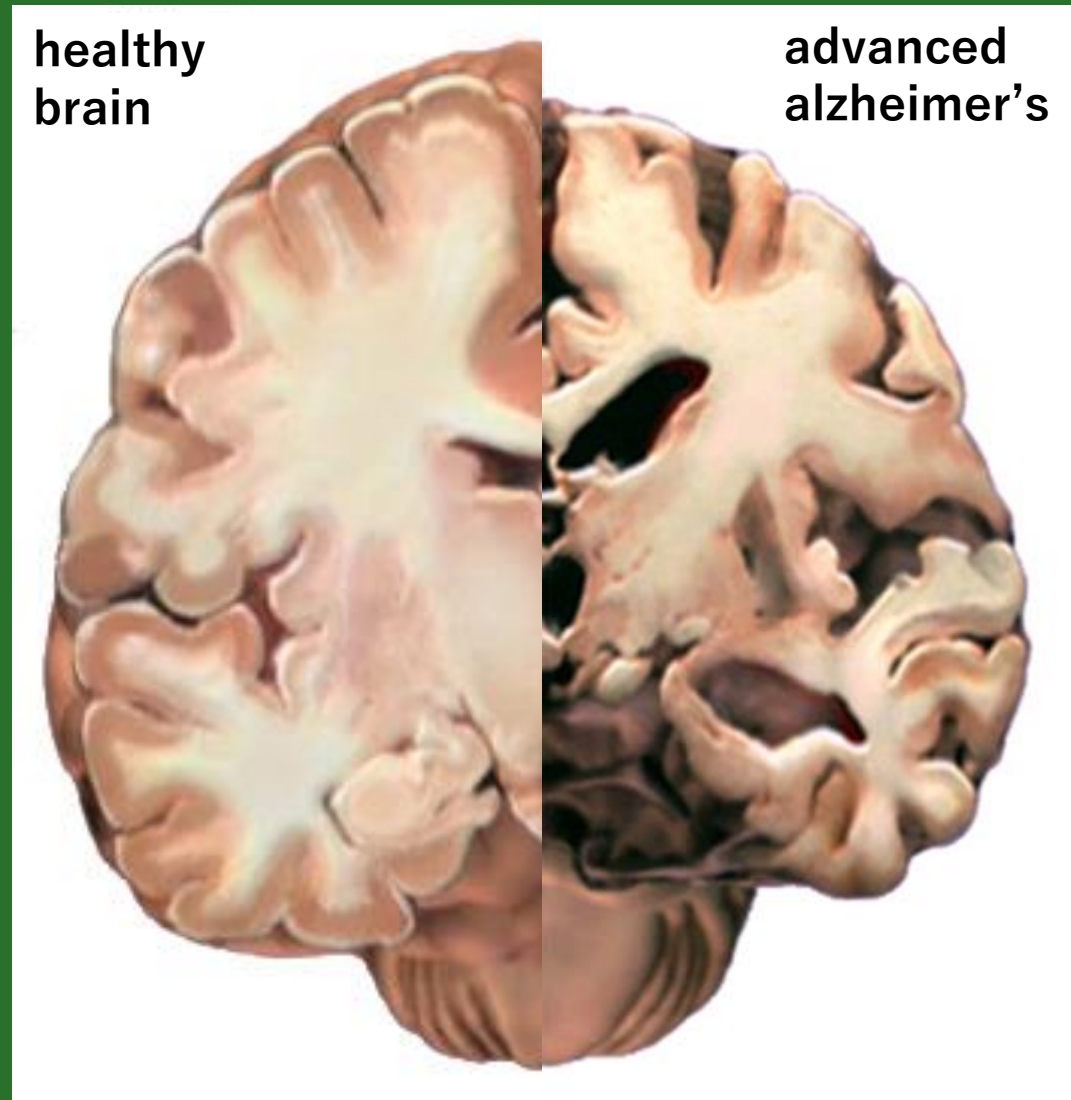


- Alzheimer's disease
- Vascular dementia
- Lewy body dementias, etc.

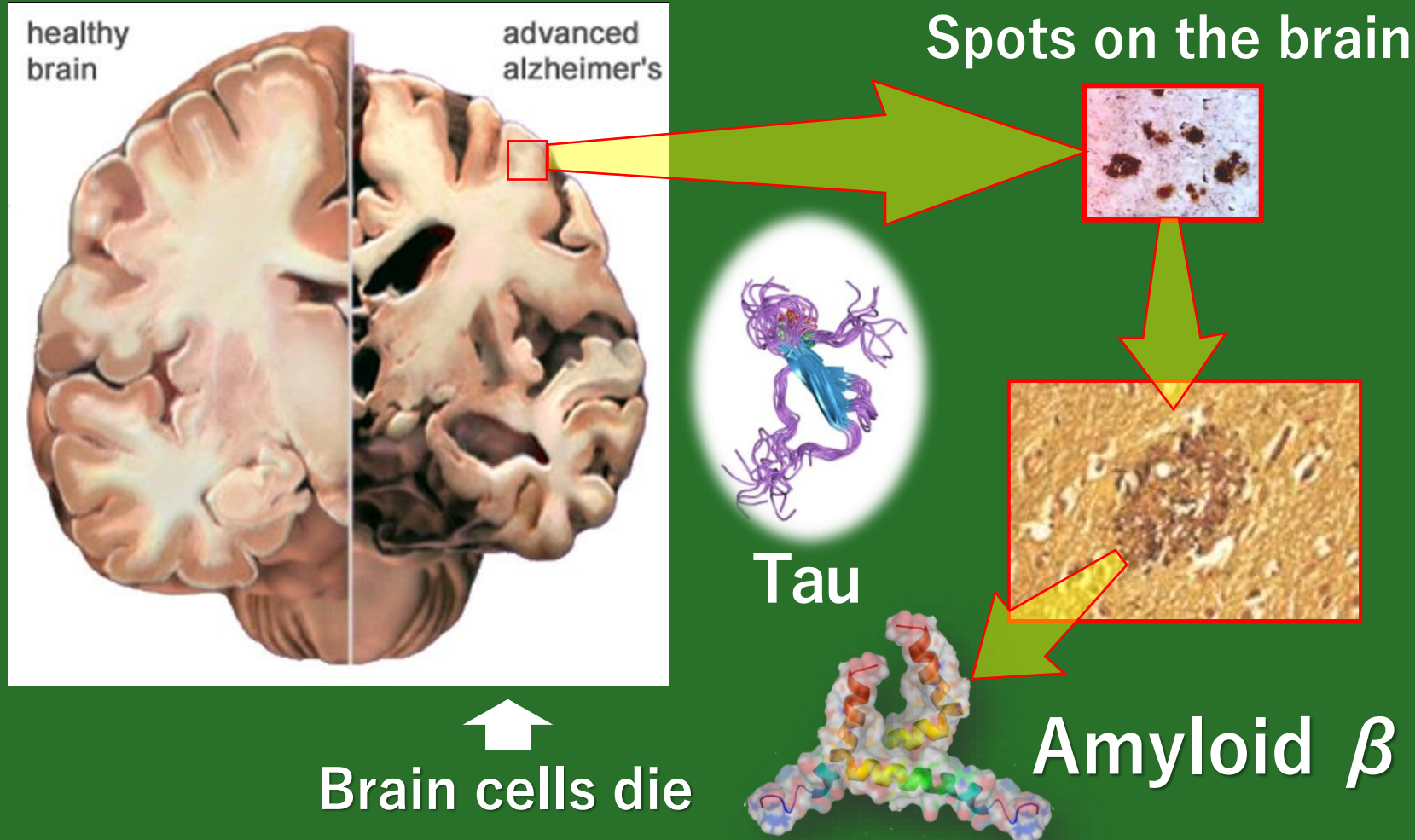


**What is Alzheimer's disease?**

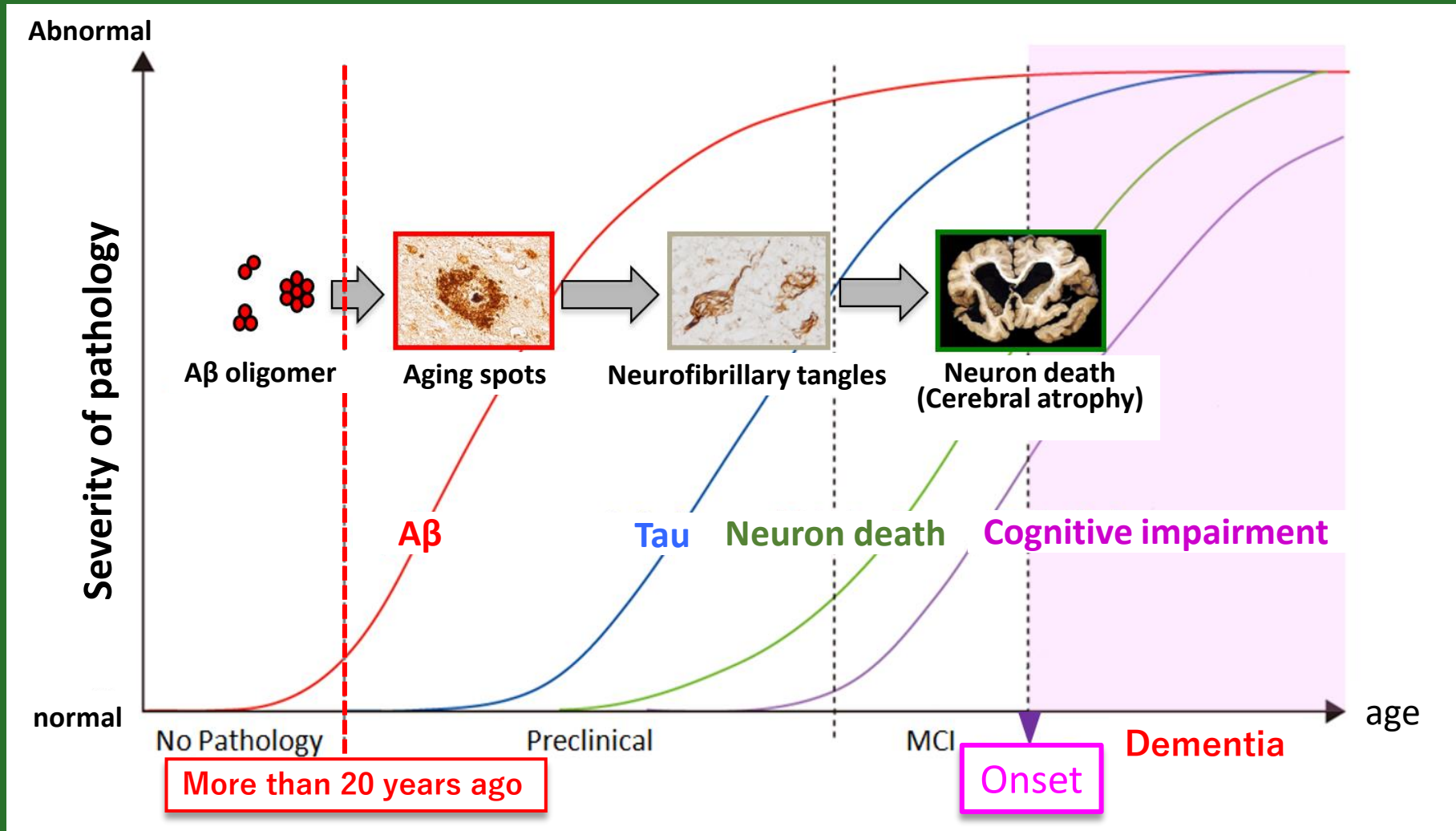
# What is Alzheimer's disease?



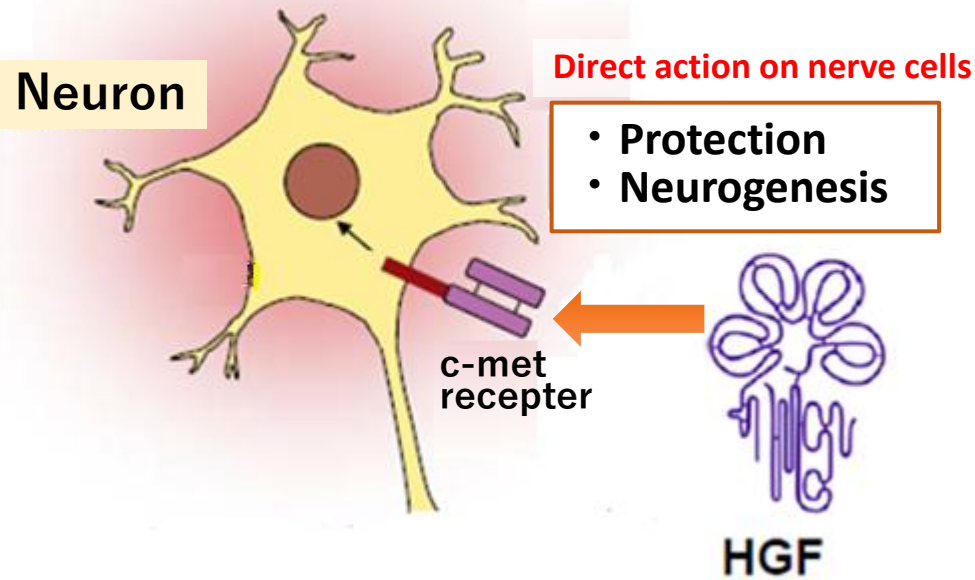
# What is Alzheimer's disease?



# The cause of Alzheimer's begins in the 40s

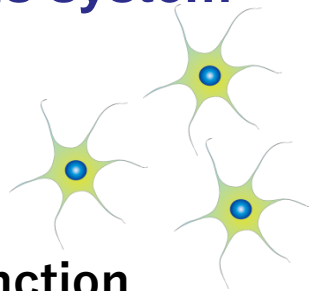


# Action of HGF on nerve cells



## Action of HGF on the nervous system

- Neurotrophic factor
- Extension of nerve cell life
- Promotion of neurogenesis
- Improvement of glial cell function
- Suppression / improvement of fibrosis (gliosis)



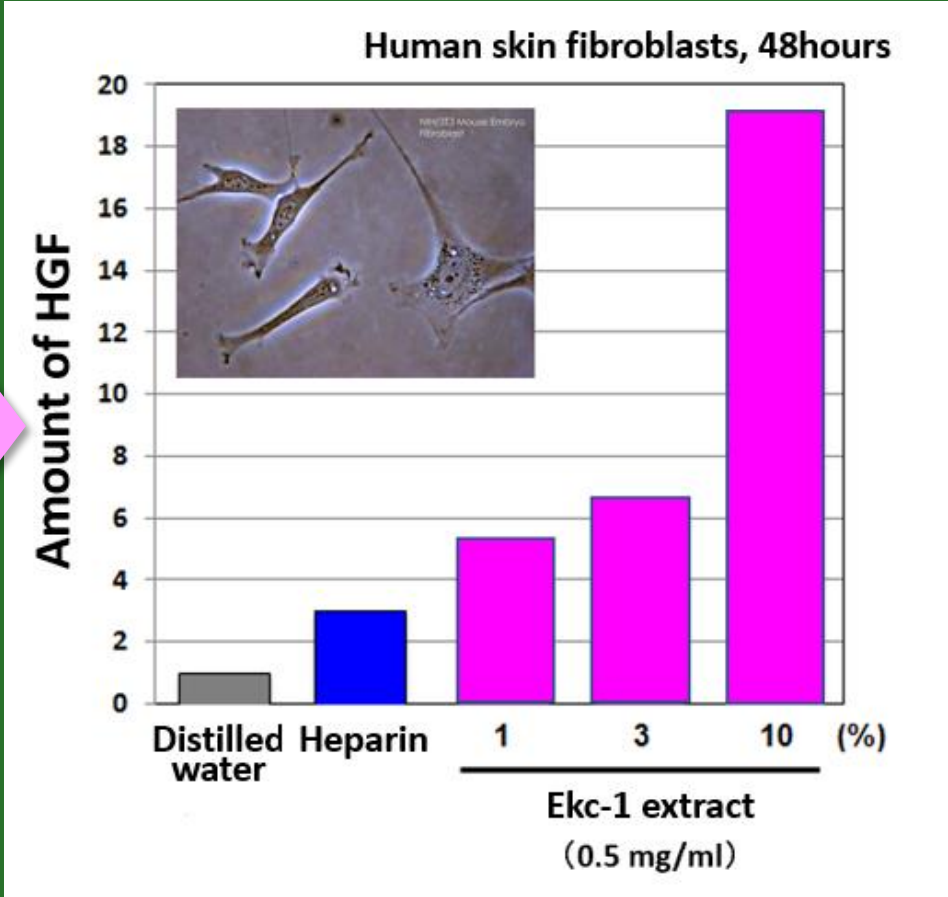
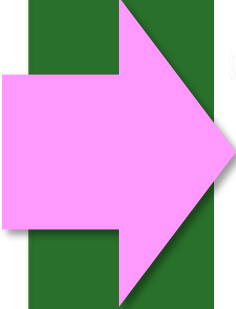
## Neurological disorders for which HGF is effective

### Disease name

- Alzheimer's disease
- ALS (Amyotrophic Lateral Sclerosis)
- Spinal cord injury
- Parkinson's disease
- Cerebral ischemia
- Cerebral infarction
- Hydrocephalus
- Huntington's disease
- Peripheral neuritis



# "Ekc-1" that induces high-level production of HGF



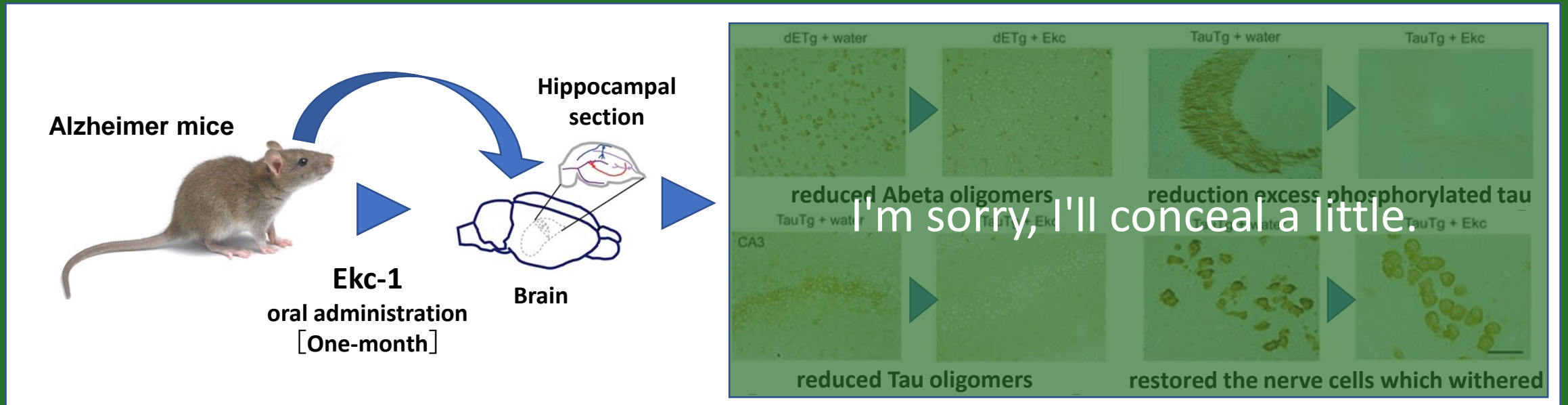
# Anti-dementia actions of Ekc-1 in AD model mice

## Abstract

We developed a new formulation of Chinese herbs which is to be used in the treatment of dementia. This formulation, referred to as Ekc-1, is expected to improve total brain functions, particularly cognitive function, in humans and is currently classified into health foods in Japan. We first tested the effects of Ekc-1 in aged people with mild cognitive impairment. Twenty people with the mean age of 79 years old were prescribed with Ekc-1 for 1 month, and their cognitive function was assessed by the Hasegawa's dementia scale-revised (HDS-R) before and after the treatment. The cognitive function of the recipients was improved from 23.95 to 27.50 in average. No adverse effects were observed. To investigate the mechanism underlying Ekc-1-induced cognitive improvement, we next examined the effects of Ekc-1 in model mice of Alzheimer's disease and tau-associated frontotemporal dementia. Ekc-1 was orally administered for 1 month to aged model mice, and their memory and neuropathology were evaluated by the Morris water maze and histological/biochemical analyses, respectively. Ekc-1 significantly reduced the levels of Aβ oligomers and tau hyperphosphorylation, rescued synaptic degeneration, and improved the memory in mutant APP transgenic mice (Alzheimer's disease model). In intron-mutant tau transgenic mice (frontotemporal dementia model), Ekc-1 significantly decreased the levels of tau hyperphosphorylation and tau oligomers, restored synapse levels, and ameliorated the memory. In addition, Ekc-1 enhanced the learning/memory in wild-type aged mice. The levels of BDNF and HGF in the brain were significantly increased in both model mice and wild-type mice. These results suggest that Ekc-1 is a good candidate of the nutraceuticals/medicines for the prevention and treatment of dementia.

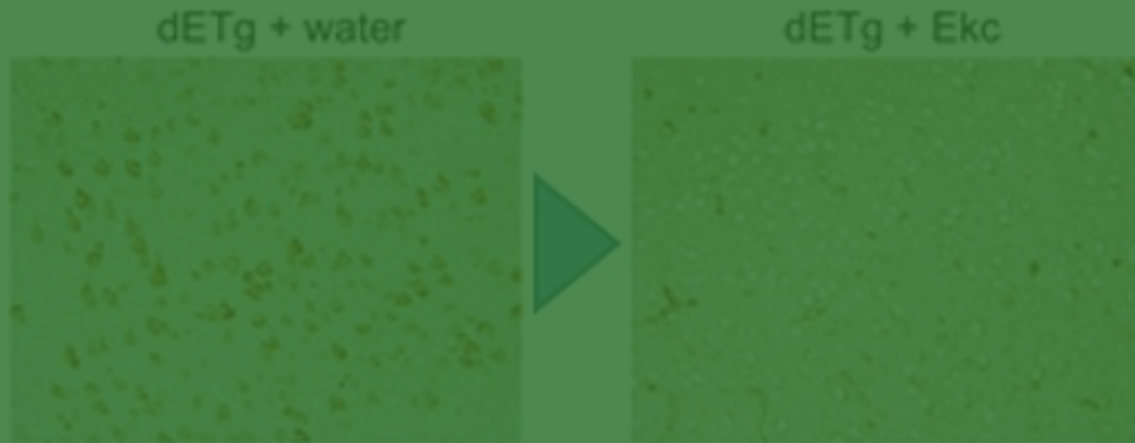
# Anti-dementia actions of Ekc-1 in AD model mice

Ekc-1 extract was orally administered to 11–14 month old AD mice for 1 month (3 mg), cognitive function test was performed, and then brain pathology was examined by histochemical and biochemical methods.



Eighty percent of dementia, mainly Alzheimer's disease, is caused by denatured proteins ( $A\beta$  oligomers, Tau oligomers, hyperphosphorylated Tau, etc.) that accumulate in nerve cells.

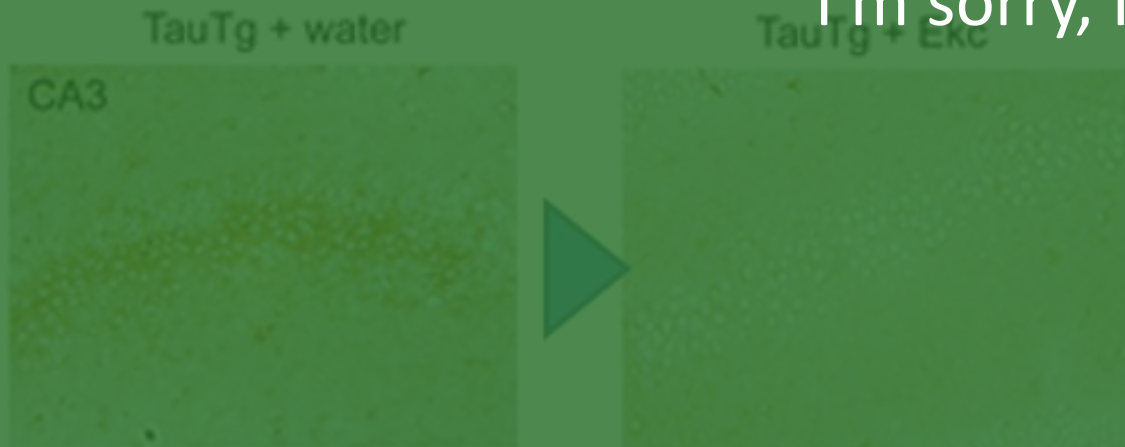
# Anti-dementia actions of Ekc-1 in AD model mice



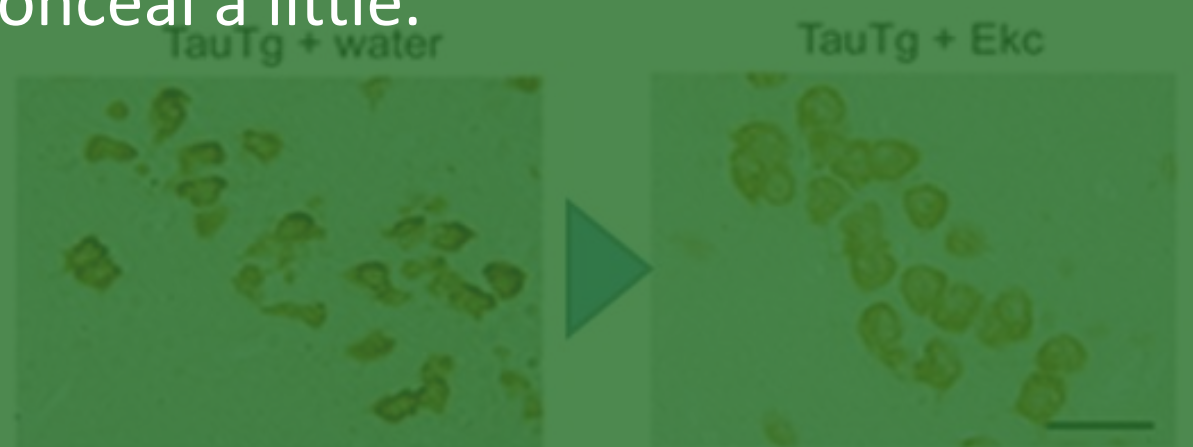
reduced Abeta oligomers



reduction excess phosphorylated tau



reduced Tau oligomers

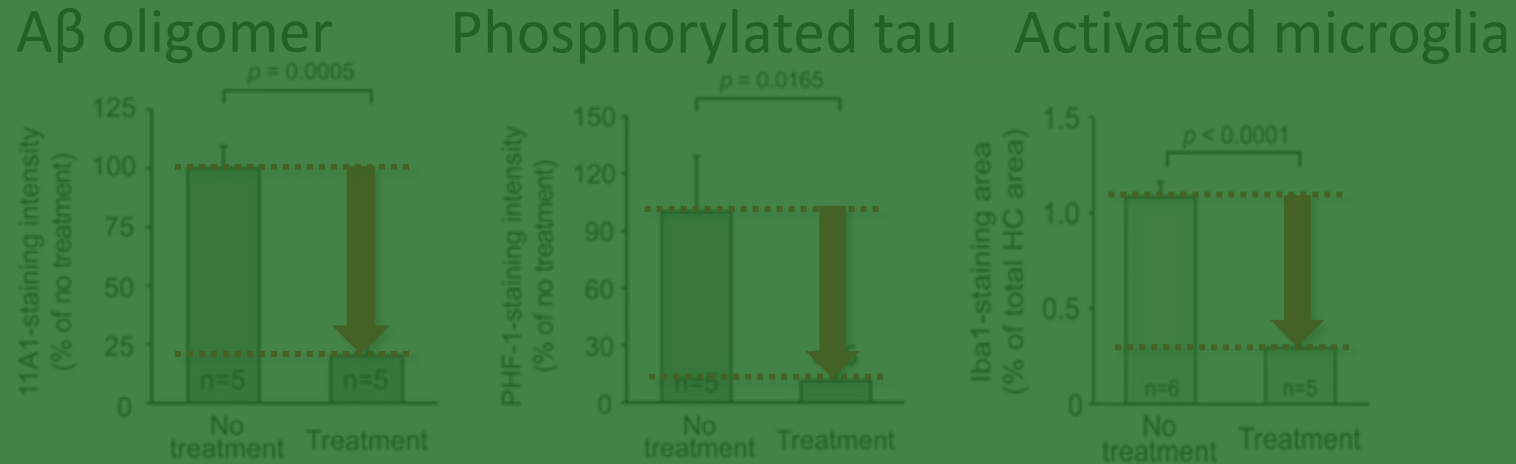


restored the nerve cells which withered

I'm sorry, I'll conceal a little.

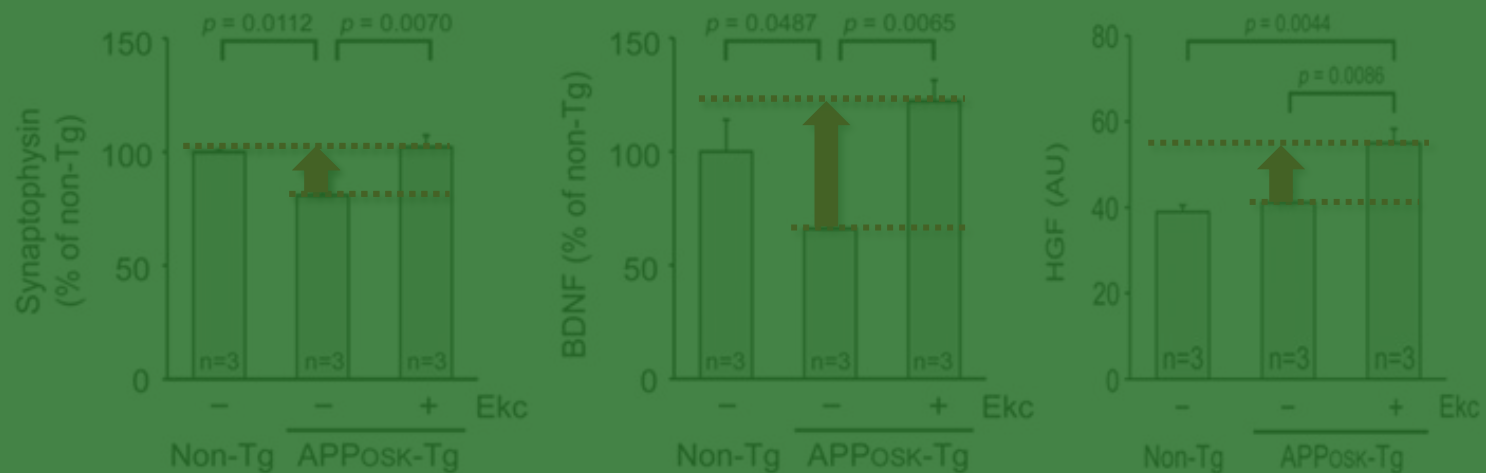


# Anti-dementia actions of Ekc-1 in AD model mice



Synaptophysin, BDNF, HGF

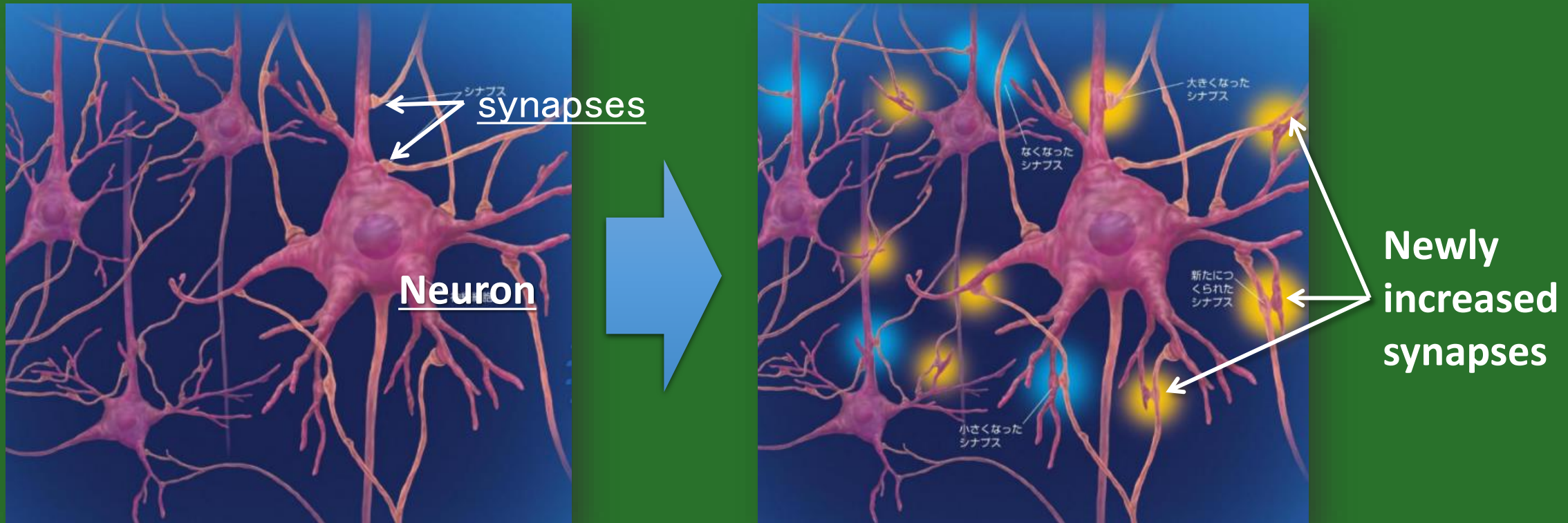
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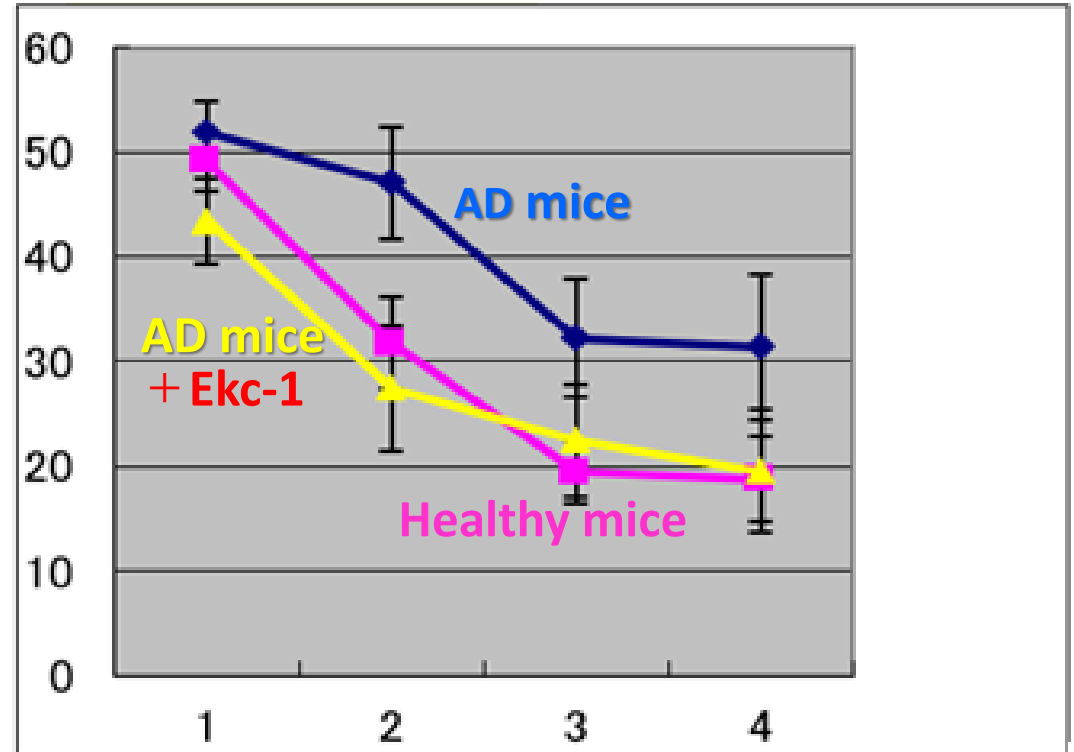
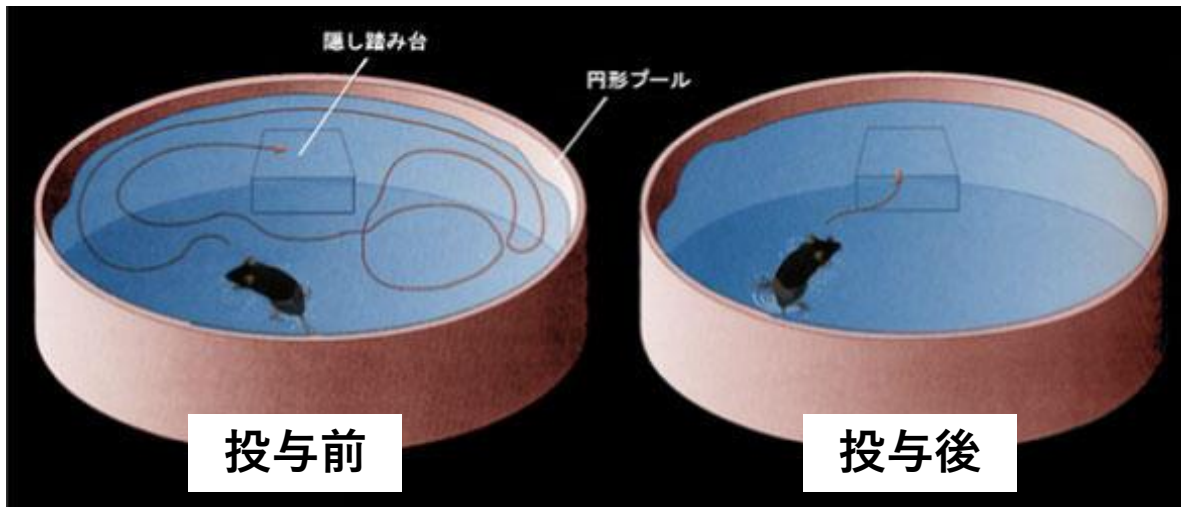
# BDNF [Brain-Derived Neurotrophic Factor]

It is a factor that regulates the growth of nerve cells such as survival, growth, and hyperactivity of synapses, and is an essential protein of the nervous system for the increase of brain cells.



# A test to measure the cognitive function (learning ability / memory ability) of mice

## Morris water maze test



Yellow ■ : Tg Ekc-1 (n = 7)  
Blue ■ : Tg water (n = 7)  
Red ■ : Non-Tg water (n = 7)

# Ekc-1 efficacy in humans

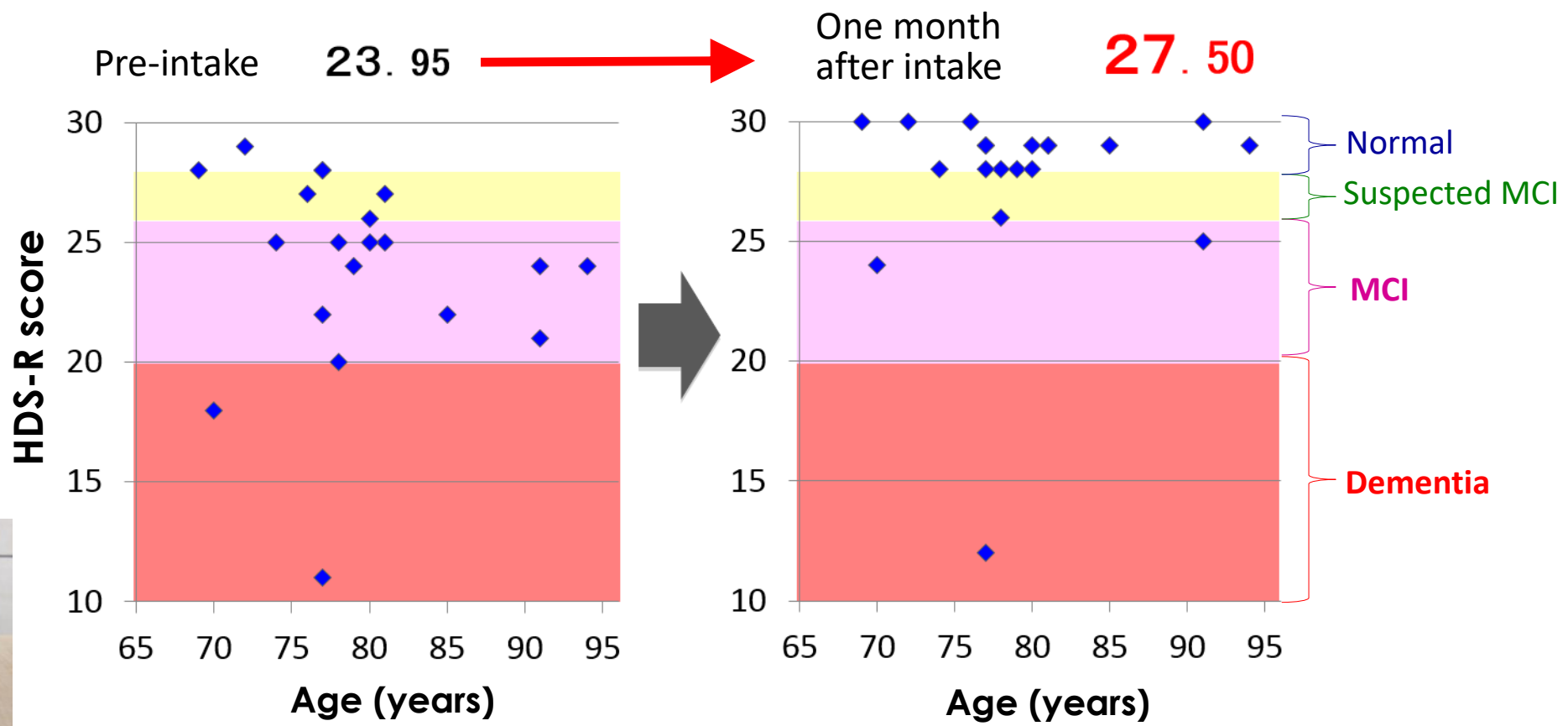
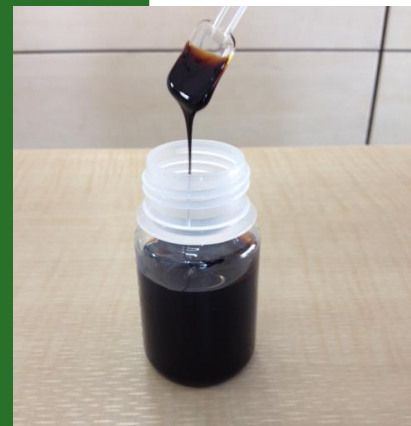


Figure HDS-R score changes following Eko-1 intake

(HDS-R: Hasegawa Dementia Scale-Revised)



Concentrated extract

Ekc-1 improves the cognitive function in humans



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人体の組織(脳)・  
細胞を再生する!

HGF

# 認知症 治療の

# 革命

西洋と東洋が出会ったとき  
もうひとつの再生医療が  
道を開いた。  
「認知症はもう  
根治しない病  
ではない。」

# Revolution in dementia treatment

HGF that regenerates human  
tissues (brain) and cells

Supervisor TOSHIKAZU NAKAMURA

Author KIYOMASA OKA

Author HIDEO OSHIRO

# Summary of Ekc-1 effect experiences-①

## 【Cranial nervous system related experiences】

- ◎ Symptoms of dementia (cognitive function / others) improved.
- ◎ Symptoms of Parkinson's disease improved.
- ◎ Prognostic symptoms at the cerebral contusion (language disorders) improved.
- My forgetfulness improved. Enhanced memory.
- My head became lighter. Eases stress.
- I was no longer frustrated and nervous.
- My anger disappeared.
- I felt brighter.
- I feel motivated
- My anxious feelings disappeared.
- I became a positive thinker
- I can sleep through the night again.
- I can wake up better in the mornings.
- Increased my concentration ability, and also my golf score.



# Summary of Ekc-1 effect experiences-②

## 【Human musculoskeletal system related experiences】

- ◎ Symptoms of spinal stenosis (back pain, walking difficulty) improved.
- The pain I had because of my cervical spondylosis is gone.
- My body became lighter and my movements became more vigor.
- It became easier to go up and down the stairs.
- My stiff shoulders improved.

## 【Internal medicine related experiences】

- ◎ Liver function improved.
- ◎ Kidney function improved.
- Even after drinking too much, I won't get a hangover.
- My weak stomach improved.
- My hemorrhoids improved.
- I stopped going to the bathroom at night.
- My limbs won't become cold anymore.

# Summary of Ekc-1 effect experiences-③

## 【Skin / hair related experiences】

- ◎ Atopic dermatitis improved a lot.
- My rough skin became moist and improved.
- My skin complexion improved.
- My grey hair turned black.
- My thin hair became thick again (※External Use)

## 【Other: Pet-related experiences】

- ◎ Cat/ aplastic anemia improved. [Animal Medical Center, Gifu University]
- ◎ Dog / allergic dermatitis (dermatitis/ hair loss) improved.
- My old dog who wouldn't walk anymore now walks again vigorously.
- My old dog (18 years old) who just slept and had no appetite became healthy and hungry again.
- The color of the fur improved.

# Medicinal plants extract "Ekc-1" that induces high-level production of HGF



# Regenerative medicine supplement "Chisei" that induces high-level production of HGF





# Other product groups containing "Ekc-1"



**Thank you for your attention!!**

**I.O.M.S**

**漢方医科学研究所**