

Growth Factor

Ella & Adam

1986's Nobel Prize
in
Physiology or Medicine

Rita Levi-Montalcini & Stanley Cohen



<https://www.britannica.com/biography/Rita-Levi-Montalcini>



<https://www.the-scientist.com/biochemist-stanley-cohen-discovered-gf-67000>

Growth Factors

- Proteins that regulate **cell growth, proliferation and differentiation**
=> essential in **wound healing, immune response and development**
- Two principal GF (of different cells) :
=> **Nerve Growth Factor (NGF)**
=> **Epidermal Growth Factor (EGF)**

Context

Human consists of **billions of cells**, but start from just **one** !

At first, all cells are the same, but later they specialize -> **differentiation**

The pattern for growth and differentiation has long been established but what about the regulation of this development ?

How does that work ?

Context

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Growth Factors

Regulation of Growth

- Cells communicate with each other via signal substances
- Many cell types synthesize these substances/ hormones to influence the cell of origin and the development of their neighbours
- Research to find the identity of the active substance -> Growth Factors
- Two major discoveries of different growth factors helped us understand better how these work

NGF

~ 1950's Levi-Montalcini moves from Italy to USA

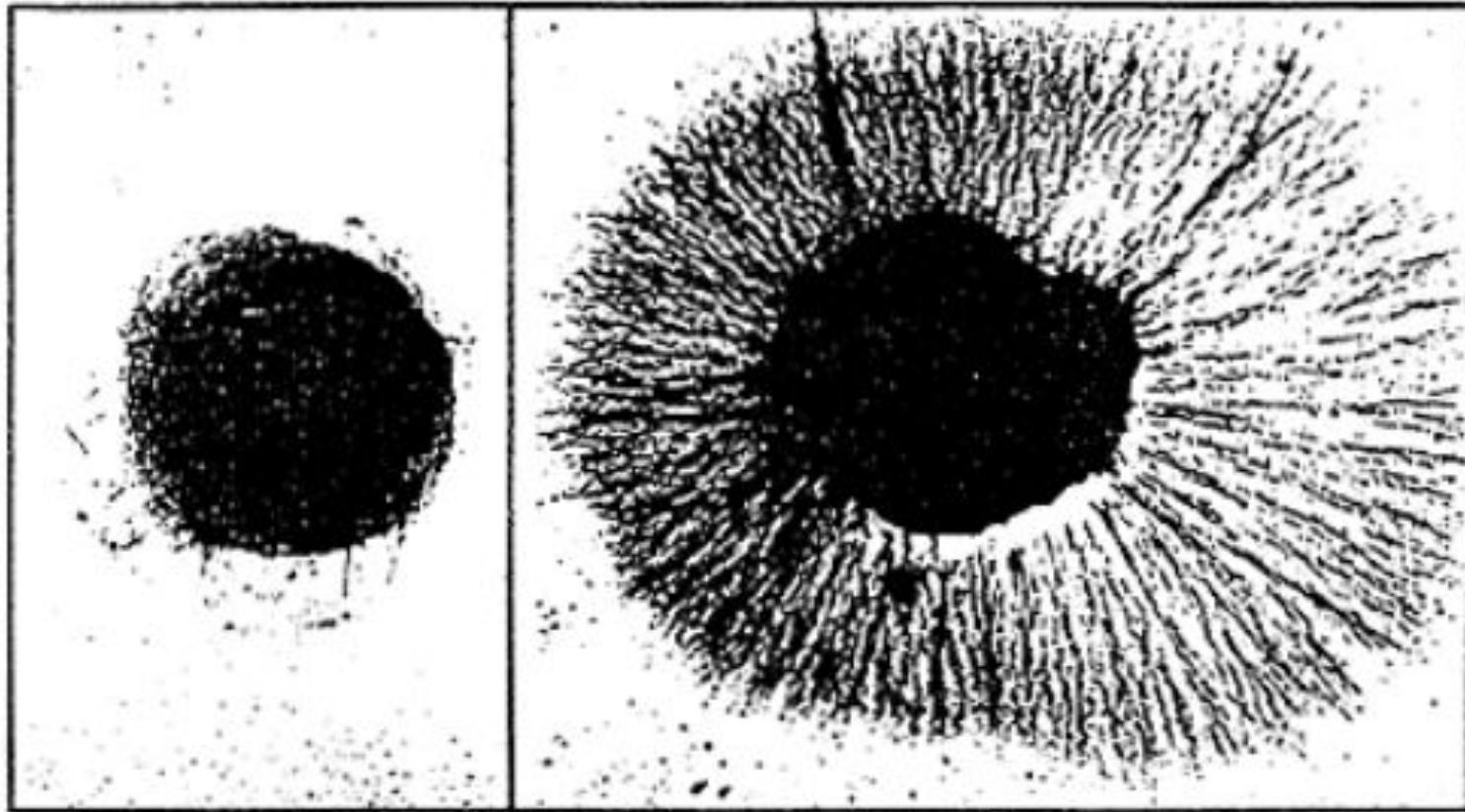
- Transplanted a **mice** tumour to **chick** embryos
- Observed a **potent growth** of the embryos **nervous system** (no contact)
- Concluded that mice tumour **releases** a nerve growing factor

=> Discovery of NGF

NGF

After more researches :

- NGF is an extremely potent biological substance (reaction after only 30sec)
- After the addition of NGF, nerve fibres start to grow out from the ganglion, and after a **day's exposure** :



NGF

1953 Stanley Cohen joins the research :

- Purified a nerve growth-promoting extract
- Contained both **protein** and **nucleic acids**
- Tried to determine which was active with venom snake (nucleic acids-degrading)
- Realised **venom snake** had more nerve growth-promoting activity than the tumour
- Started to look for more and also found the **salivary gland in male mouse**

NGF

Conclusion :

- They discovered NGF consists of **118 amino-acids**
- Also purified the **antibody** NGF, inhibit growth
- Found in mammals, birds, reptiles, amphibians and fishes
- Nerve fiber **grows toward** the source of NGF

=> Tissues attract nerve fibers by sending out NGF

EGF

During the study of NGF :

- Injected **salivary gland extract to newborn mice**
- Observed unexpected acceleration of development (**eyes and tooth**)
- Not nerve => there is **another substance** than NGF in salivary gland extract
- Named it **Epidermal Growth Factor** (because stimulated **epithelial cells**)
- Realised it's responsible for a lot of events :
=> stimulation of glucose and amino-acid transport, activation of protein synthesis, initiation of cell replication, ...

Signal from outside reaches inside of the cell

- Presence of specific binding sites (receptors) on surface of target cells essential for action of EGF
- Receptors catch EGF and EGF-receptor complex is taken into the cell
- Discovery of special genes, oncogenes: proto-oncogene becomes more active than normal in the cell growth and division

Impact

Levi-Montalcini and Cohen created a **new-school** with their discoveries.

More growth factors were discovered with the years :

- VEGF, BDNF, PDGF, ...

Human studies on growth factor

Today there are a lot of GF studies for human application :

- **NGF** : **pain, neurodegenerative diseases** (Alzheimer) / side effects (e.g. pain sensitization)
- **VEGF** (Vascular Endothelial Growth Factor) : **stimulate blood vessel growth, wound healing and cardiovascular diseases**, used in cancer therapies to **block blood supply to tumors**

Human studies on growth factor

- **EGF** : skin regeneration, ulcer treatment, and corneal injuries
- **BDNF** (Brain-Derived Neurotrophic Factor) : depression, neurodegenerative diseases, and rehabilitation after stroke (early phases)

Questions ?