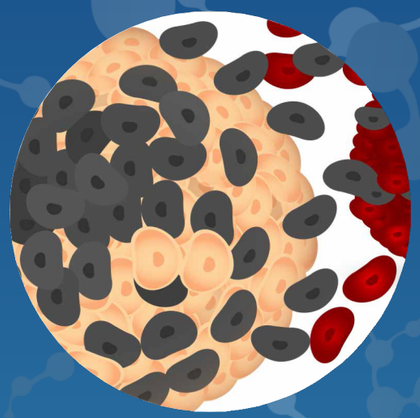
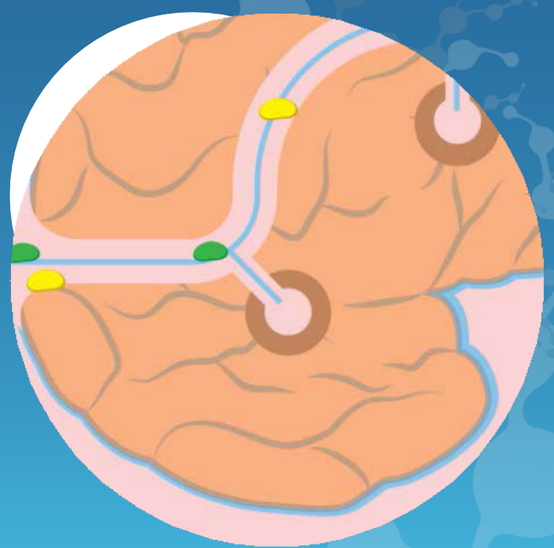
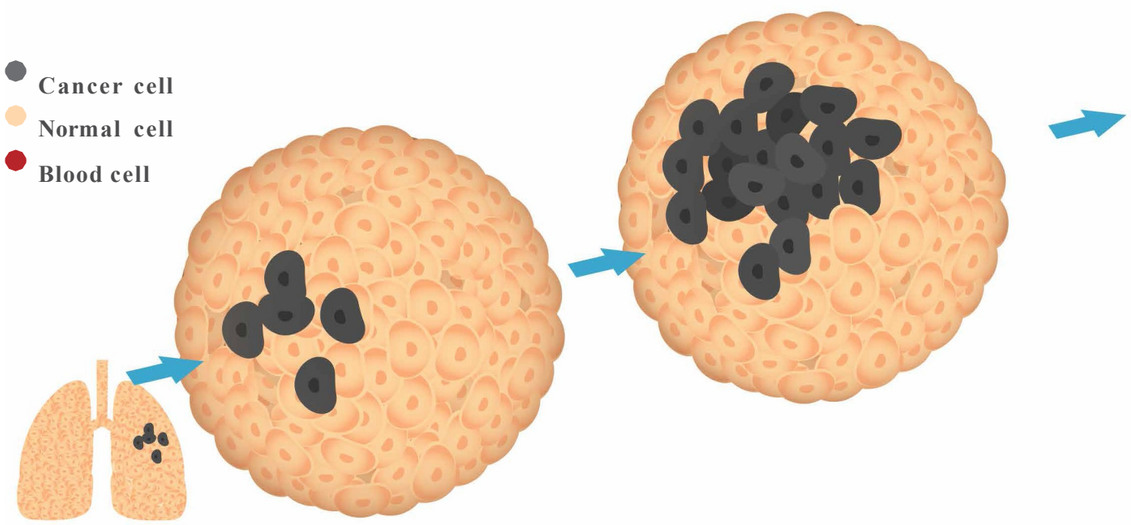
Propanc
Biopharma, Inc.

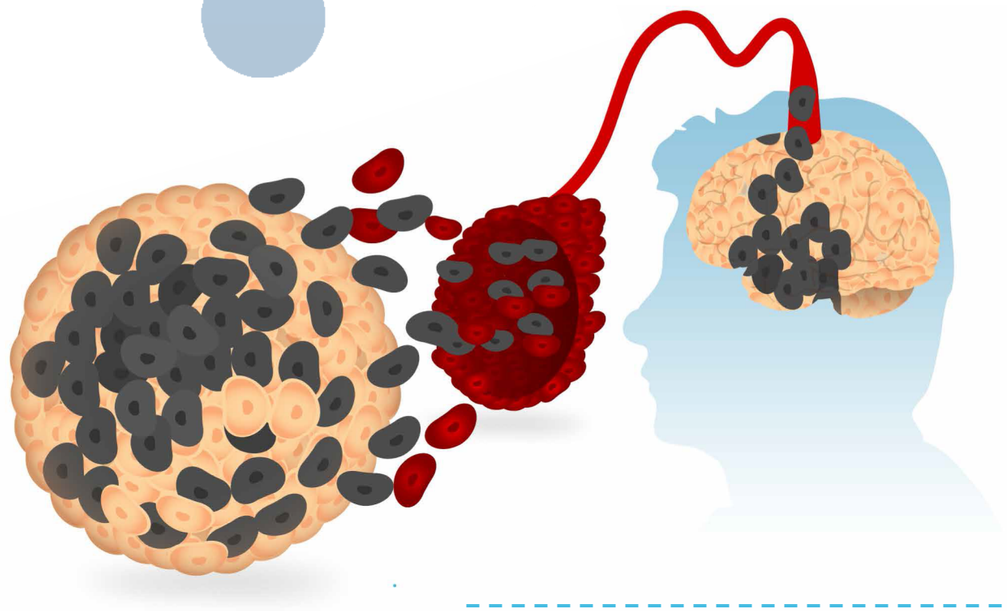




# Everybody knows what cancer is

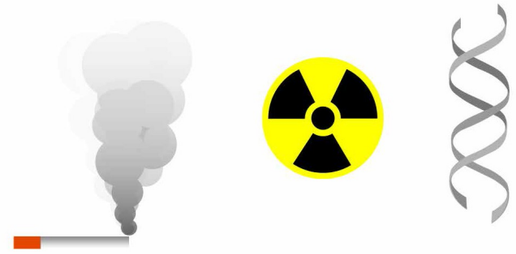
Cells in the body that start to divide rapidly and uncontrollably, with an ability to migrate from one location and spread to distant sites.



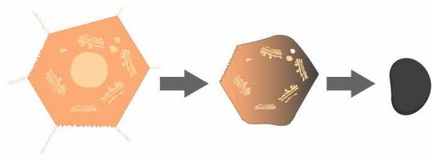
We all know someone who has suffered from this disease

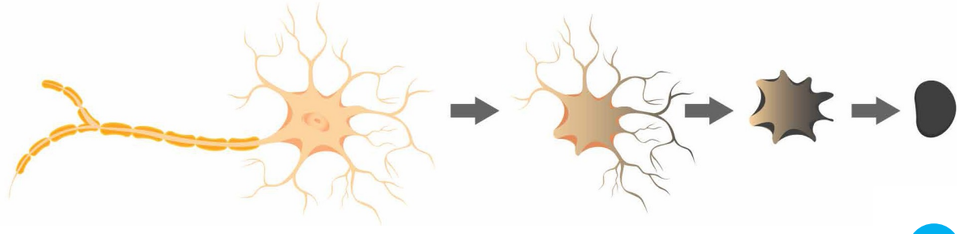
There are many factors which increase your risk of getting cancer.



# But why does a cell become cancerous?

Because a cell becomes undifferentiated. In other words, the cell forgets how to do its job and invests all its energy in proliferating. Unlike normal cells, cancer cells multiply, but do not differentiate.

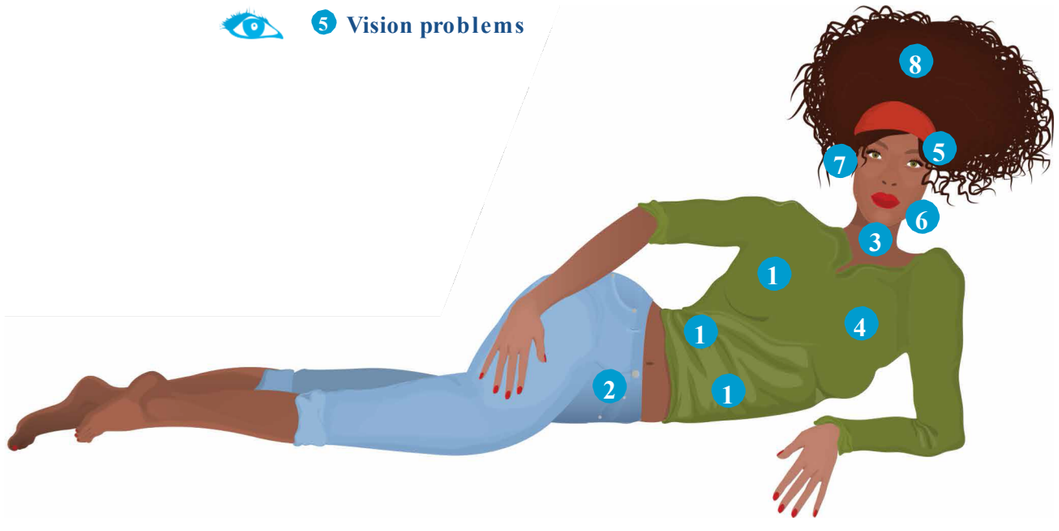




# How do common cancer therapies work?

These therapies take advantage of the uncontrolled proliferation of the cancer cells and kill these cells by targeting the cell division machinery. These therapies are effective but affect healthy cells as well, particularly those with a high rate of cell turnover, inducing undesirable side effects.

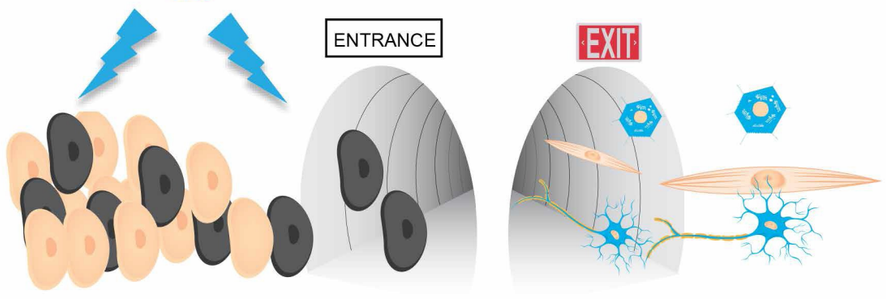
1. **Lung, liver, or kidney problems**
2. **Fertility issues**
3. **Thyroid problems**
4. **Heart problems**
5. **Vision problems**
6. **Dental problems**
7. **Hearing loss**
8. **Loss of hair**



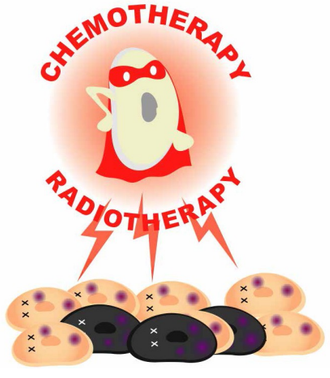



# What if the best way to stop cancer is not targeting tumor cell death, but inducing cell differentiation?


This is known as differentiation therapy.
The key question here is to convince the malignant cells to stop proliferating and return to do their work as a specific cell type.




# Advantages of differentiation therapy over conventional therapeutic strategies




Differentiation therapy does not target cell death, so healthy cells within the patient will not be compromised, unlike chemotherapeutic drugs or gamma irradiation.

Differentiation therapy induces the cancer cells into the pathway of terminal differentiation and eventual senescence.

Differentiation therapy acts not only against cancer cells, but interestingly can turn cancer stem cells (undifferentiated cells) towards completely differentiated (i.e. normal) cells.

# What lesson can we learn from our own body?

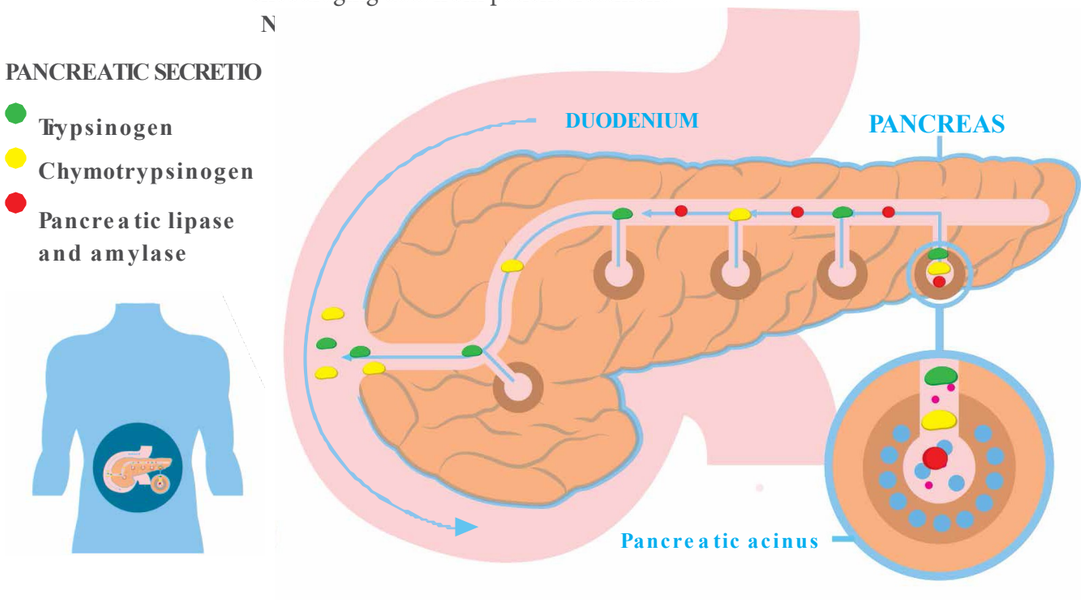
## Are there any natural elements within our organism that could help us fight against cancer?

As a matter of fact, yes there are: the enzymes, which are natural proteins that stimulate and accelerate biological reactions in the body. Particularly, the enzymes secreted by the exocrine pancreas that are essential for the digestion of proteins and fats.

**Pancreatic Enzyme Therapy:**
An old story with promising implications

More than one hundred years ago, Professor John Beard first proposed that the pancreatic enzymes represent the body's primary defence against cancer and would be useful as a cancer treatment.

Since then, several scientists have endorsed Beard´s hypothesis with encouraging data from patient treatment.






# What are we offering?

**PROPANC** is developing a long-term therapy based on a pancreatic proenzyme formulation to prevent tumour recurrence and metastasis, the main cause of patient death from cancer.

**PRP**, is a novel, patented, formulation consisting of two proenzymes mixed in a synergetic ratio.

## What we have achieved

After extensive laboratory research and a limited amount of human testing, we have evidence that PRP:

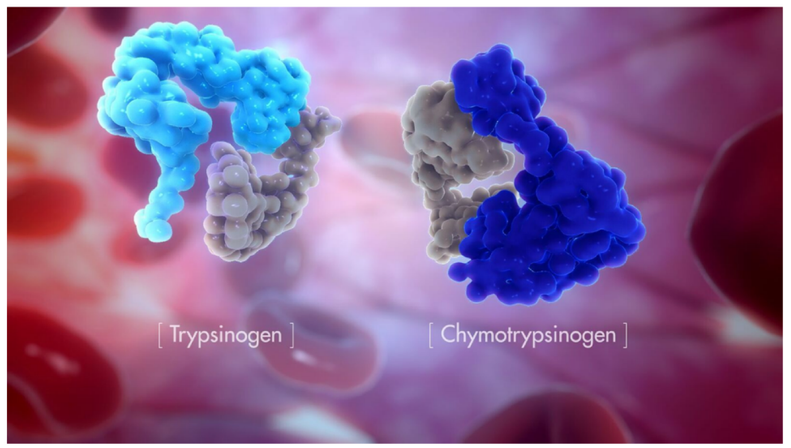
- Reduces cancer cell growth via promotion of cell differentiation;
- Enhances cell adhesion and may suppress metastasis progression;
- Has no serious side effects and improves patient survival.

# Presenting PRP

Mixture of 2 proenzymes, trypsinogen (T) & chymotrypsinogen (C) from bovine pancreas.

A synergistic ratio of 1:6 inhibits growth of most tumor cells.

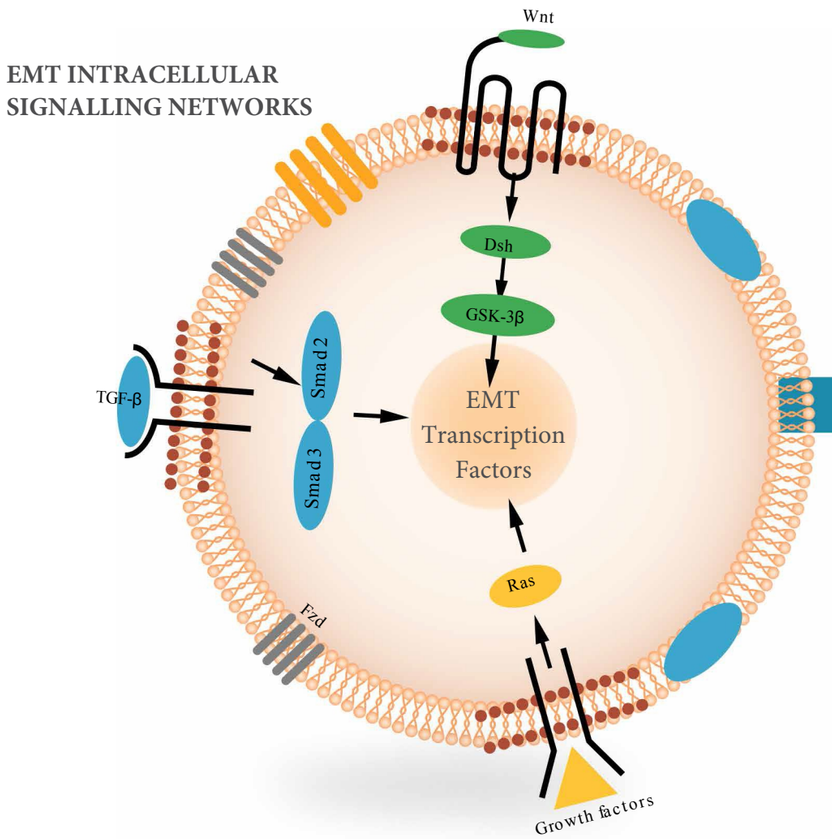
- Examples include kidney, ovarian, breast, brain, prostate, colorectal, lung liver, uterine and skin cancers.



# Pancreatic pro-enzyme therapy: Mechanism of action

## Why does metastasis occur?

Because a program inside the cell called the Epithelial-Mesenchymal Transition (EMT) is activated, which causes epithelial cancer cells to become invasive and stem cell-like, features which then allow these cancer cells to spread and metastasize.

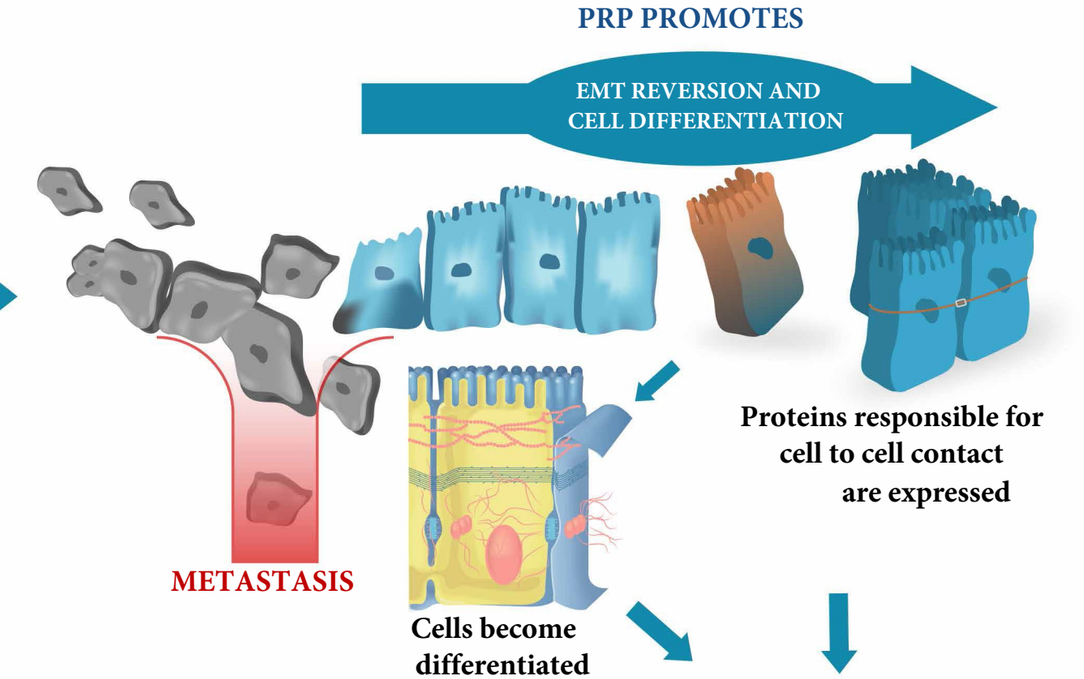





# What does PRP do?

**Reverses** the conversion from an epithelial to a mesenchymal phenotype and, as such, may reduce the metastatic potential of the tumor cells.

**Promotes** the acquisition of a less malignant phenotype in addition to a decrease in proliferation due to lineage specific cellular differentiation.




Perán M. et al., Cellular Oncology. 2013; 36(4): 289–301

Perán M. et al. Scientific Reports. 2017.; 7(1):13998.

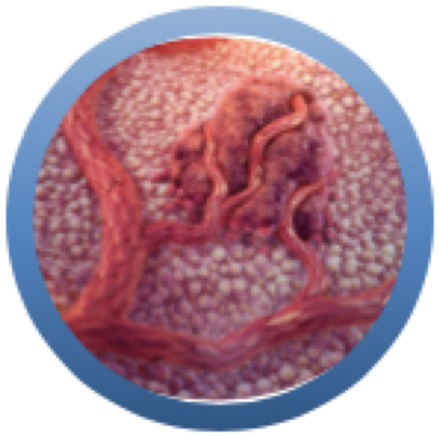
# Cancer Stem Cells – Frontier

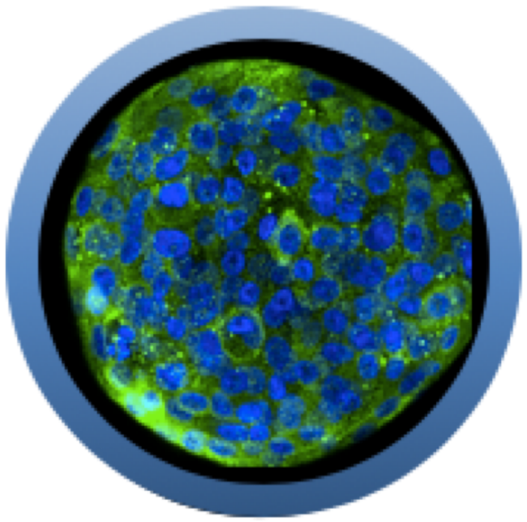
To achieve total victory, we need to eradicate Cancer Stem Cells (CSCs).

Why? Cancer Stem Cells are resistant to standard treatments because they remain dormant for long periods, then migrate to other organs, and trigger explosive tumor growth, causing the patient to relapse.

~80% of cancers are from solid tumors and metastasis is the main cause of patient death.

Our unique patented approach is designed to target and eradicate cancer stem cells not killed by radiation or chemotherapy



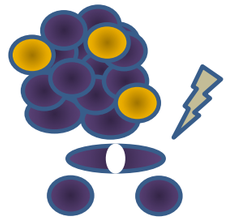




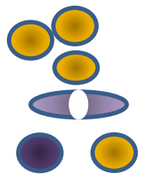
# How does PRP work against CSCs?

PRP is designed to target and eradicate cancer stem cells not killed by radiation or chemotherapy.

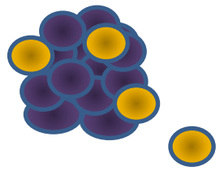
Traditional Cancer Therapies: act on tumor replicating cells, but not CSCs



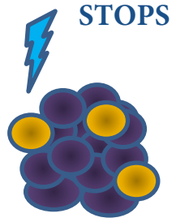
….so, CSCs can re-build the tumor mass



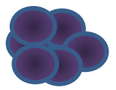
… and CSCs can migrate to start a new tumor in another orgam



PRP Therapy: **STOPS CSCs**



Tumour loses ability to generate new cells and



…. tumor disapears

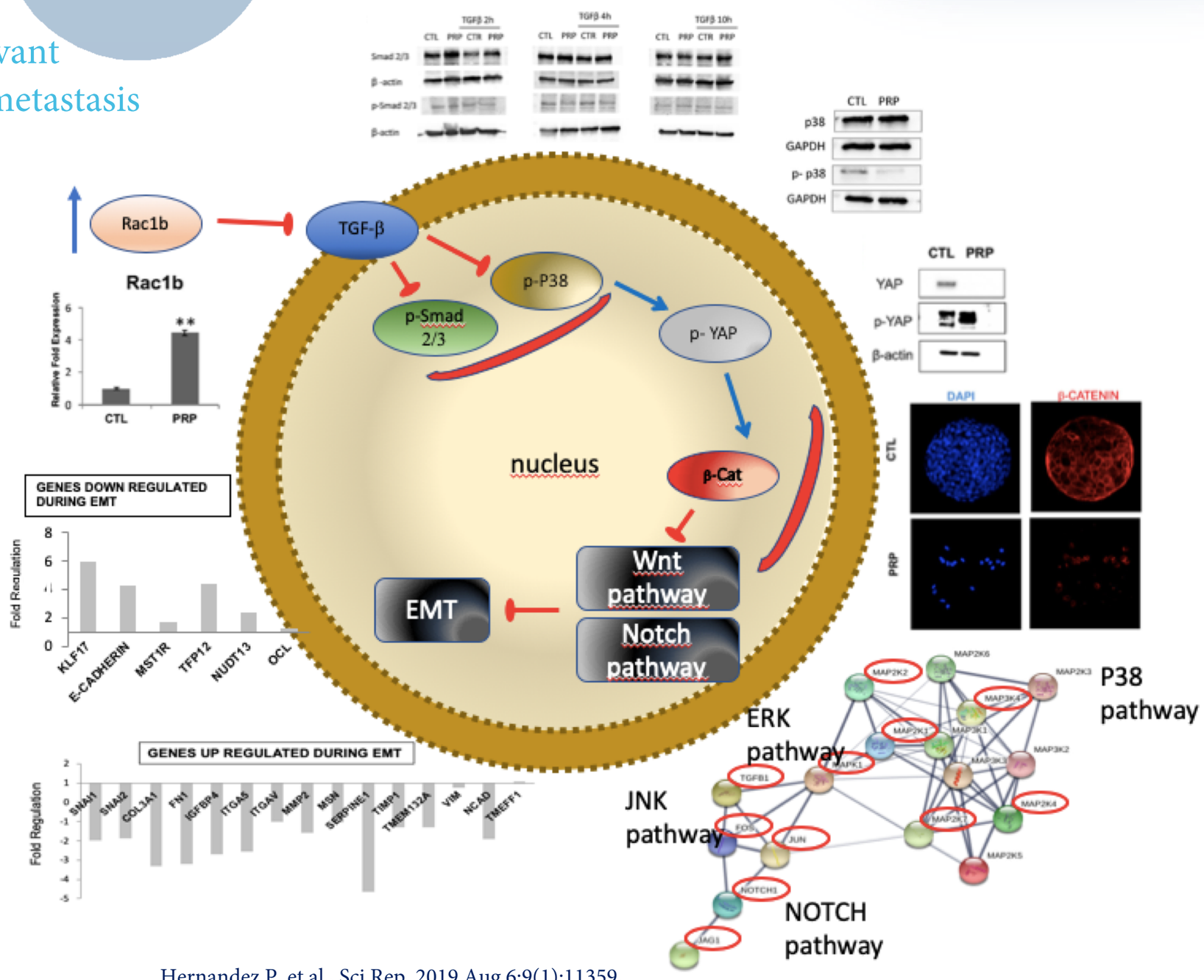
**…with no option to form a metastatic tumor elsewhere**

# PRP treatment regulates up to four relevant pathways related to cancer spread and metastasis of Cancer Stem Cells (CSCs)

## PRP acts on TGFβ, Hippo, Wnt and Notch pathways

PRP treatment promotes the up-regulation of RAC1b which avoids the hyper-activation of the p38 pathway induced by the TGF-B pathway, leading to the phosphorylation of YAP, which sequesters B-catenin in the cytoplasm, blocking the canonical Wnt pathway and inhibiting the Notch pathway.

That cascade of reactions implies the disruption of the CSC phenotype and the reversal of the malignant epithelial to mesenchymal transition process that leads to tumour invasion



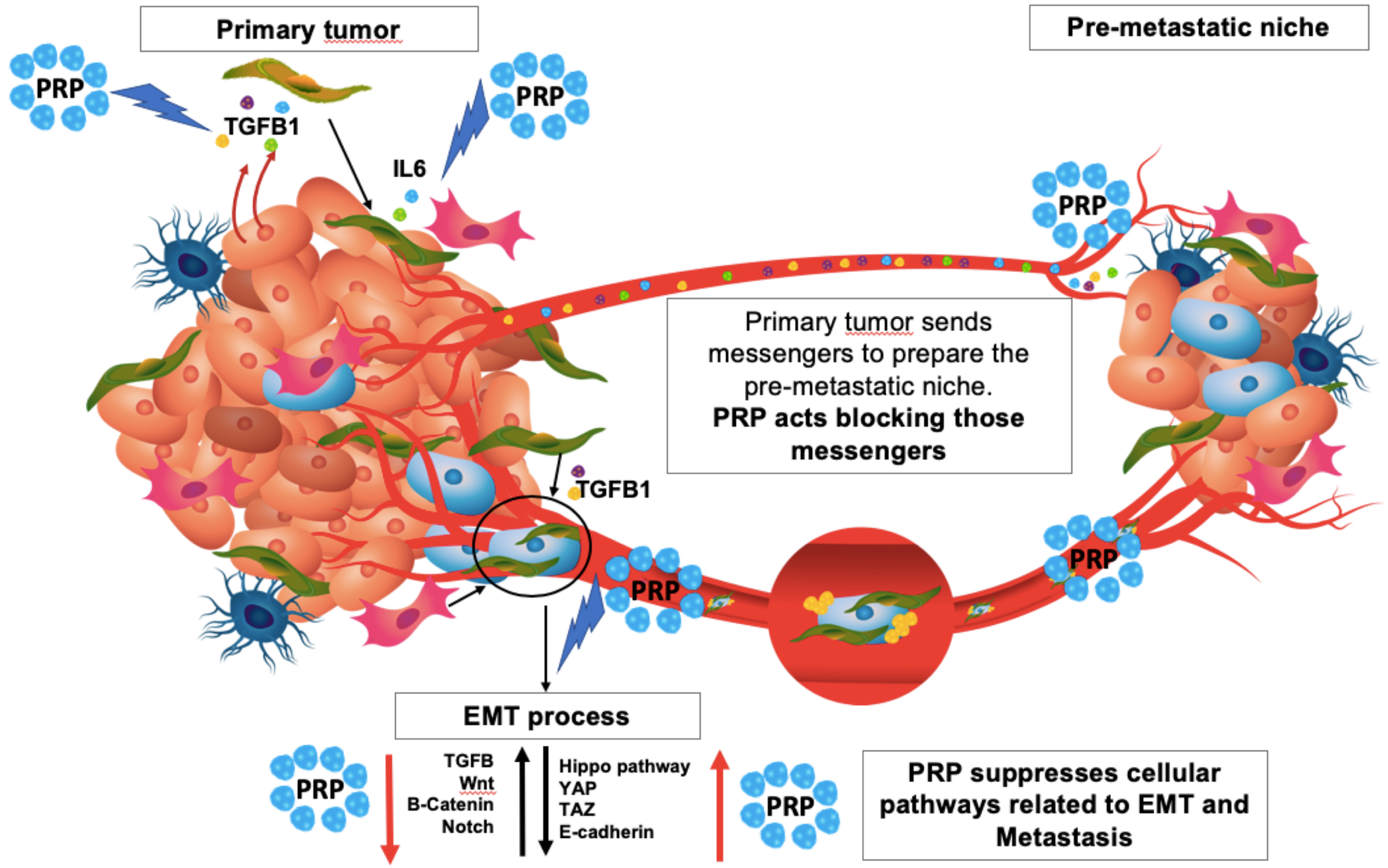

Hernandez P. et al., Sci Rep. 2019 Aug 6;9(1):11359.

# PRP impaires niche formation and tumor initiation

## How is PRP preventing metastasis?

The proenzyme treatment inhibits the expression of genes related to the CSC phenotype, changing the nature of these malignant cells toward a more differentiated and less dangerous cellular condition.

PRP interferes with the signals that the primary tumour sends to other tissues to prepare the pre-metastatic niche.



# The Company

Our novel cancer treatment is based on the original work undertaken by John Beard, a professor of embryology at Edinburgh University nearly 100 years ago, using fresh pancreatic enzyme extracts.

Through advancements in science and technology, we plan to commercialize an improved version of this hypothesis and market it worldwide.

We are an experienced team of professionals with deep clinical and scientific expertise in the development of new treatment approaches in oncology.



# Highlights

## Key features

Global demand for effective, safe and easy to administer cancer treatments is increasing rapidly;

Propanc addresses the global, unmet medical need to combat solid tumor recurrence and metastasis.

Propanc is building a robust IP portfolio around its scientific understanding of the effects of proenzymes in cancer, identifying new formulations, new routes of administration and potential new therapeutic targets.

## Market opportunity:

Growing demand for new cancer treatments as a result of a rapidly ageing population and changing environmental factors in western countries. According to the World Health Organization, all cancers (excluding non-melanoma skin cancer) are expected to increase from 8.2 million annual deaths in 2012 to over 10 million annual deaths by 2020, exceeding 13 million annual deaths by 2030.

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Website: www.propanc.com

The information is based on published research:

*"In vitro treatment of carcinoma cell lines with pancreatic (pro)enzymes suppresses the EMT programme and promotes cell differentiation".*

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Hernandez P. et al., Sci Rep. 2019 Aug 6;9(1):11359.

The text has been adapted by Professor Perán.



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*Illustrations by Tomás Justicia*