

## BRAIN TUMOR RESEARCH PROJECTS

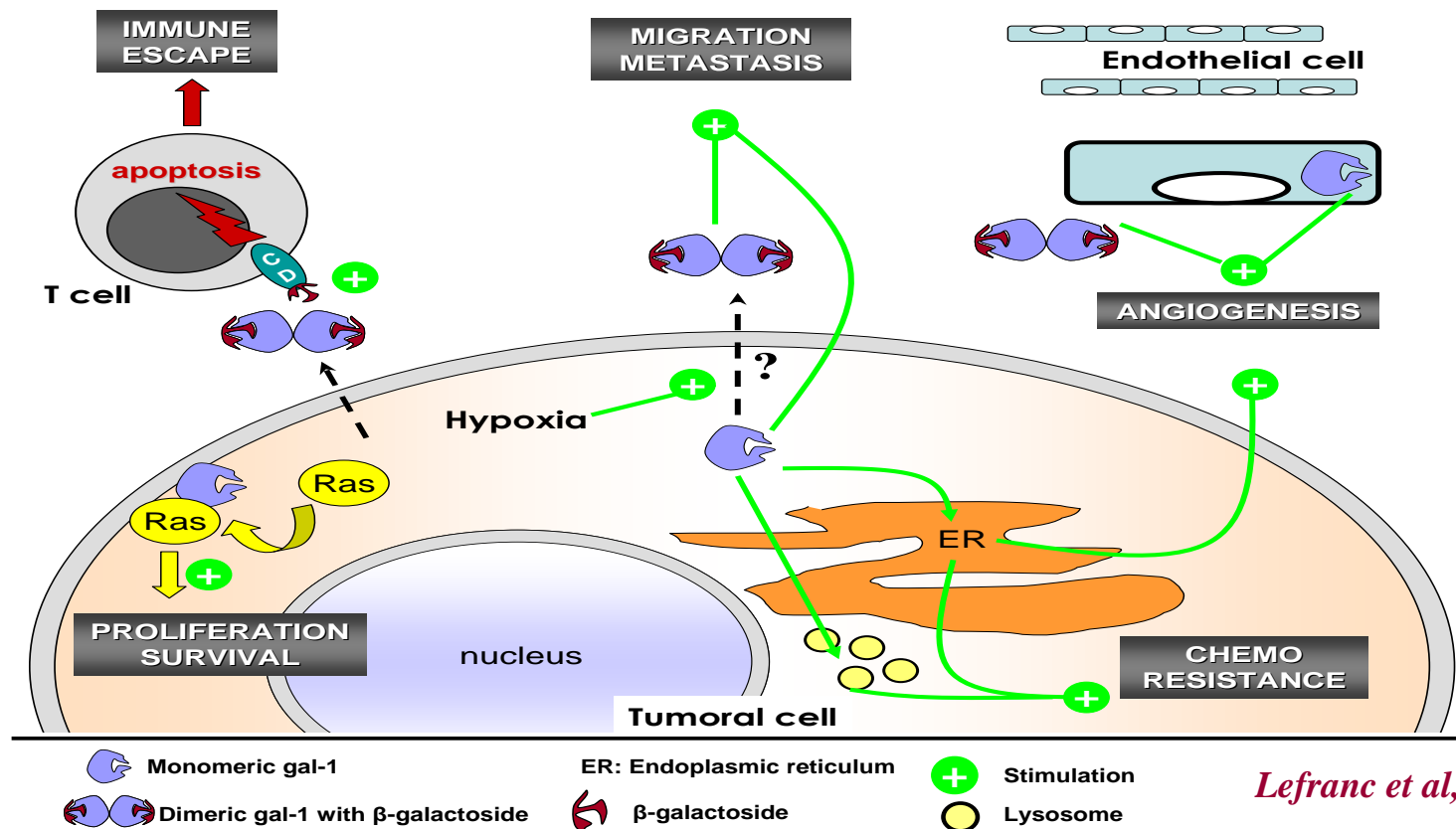


Laboratory of Toxicology, Pharmacy Faculty, ULB  
Véronique Mathieu, MD, PhD



# Anti-galectin-1 strategy

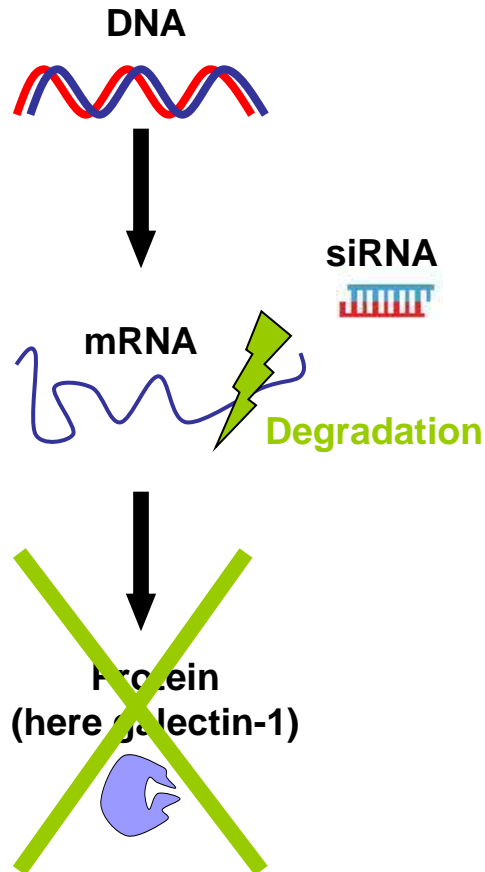
- Galectin-1 is a non vital protein that binds to beta-galactosides extracellularly and proteins intracellularly
- Galectin-1 is overexpressed by several cancer types including gliomas
- Galectin-1 favors tumor development:



# Anti-galectin-1 strategy

- Our strategy: use of siRNA that regulates the gene expression:

## Principle



➤ A patent has been taken

➤ The efficacy in the animal models showed that this approach can be used **in combination with chemotherapy** (temozolomide in particular).

➤ The roles of galectin-1 in immune escape make this anti-galectin-1 approach promising also **in combination with vaccinotherapy** (proof of concept and efficacy demonstration in collaboration with Pr De Vleeschouwer).

➤ **Ongoing**: siRNA are rapidly degraded in the human body. Formulation and targeting of the siRNA are required to improve the efficacy. (in collaboration with Pr De Vleeschouwer).

# Drugs from natural sources: narciclasine and analogs

Hippocrates of Kos (ca. B.C. 460-370) used the oil of *Narcissus* in the treatment of uterine tumors

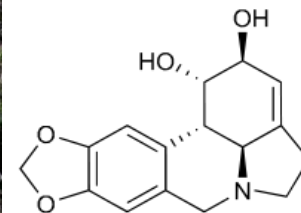
Oil of *Narcissus* was used by African, Middle American and Chinese doctors in traditional medicine

Dioscorides (40-90) used diverse *Narcissus* for skin diseases

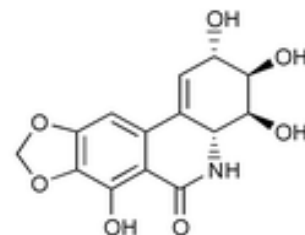


*Narcissus tazetta*

Lycorine was isolated in 1877

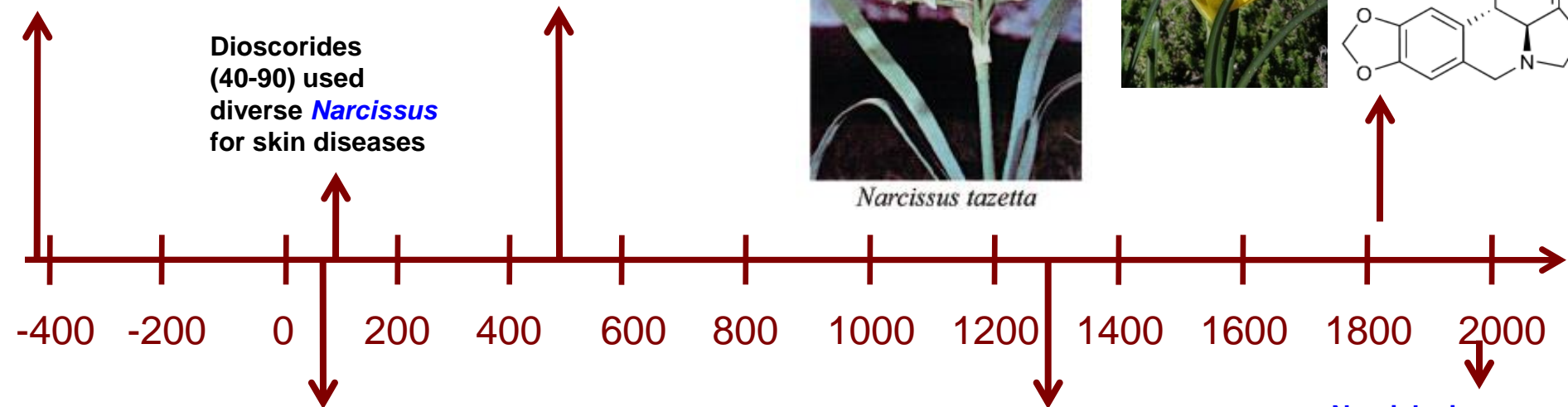


Narciclasine was isolated in 1967



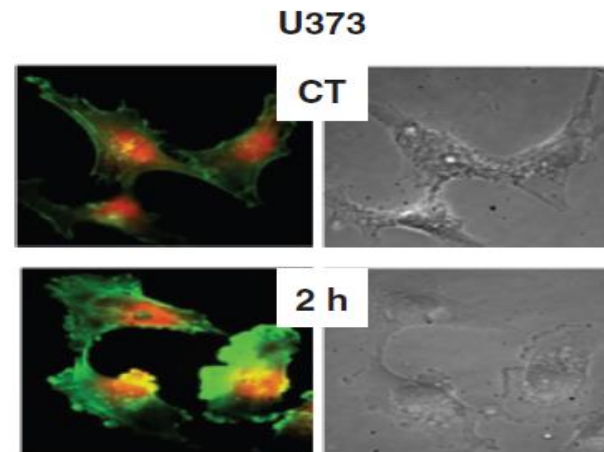
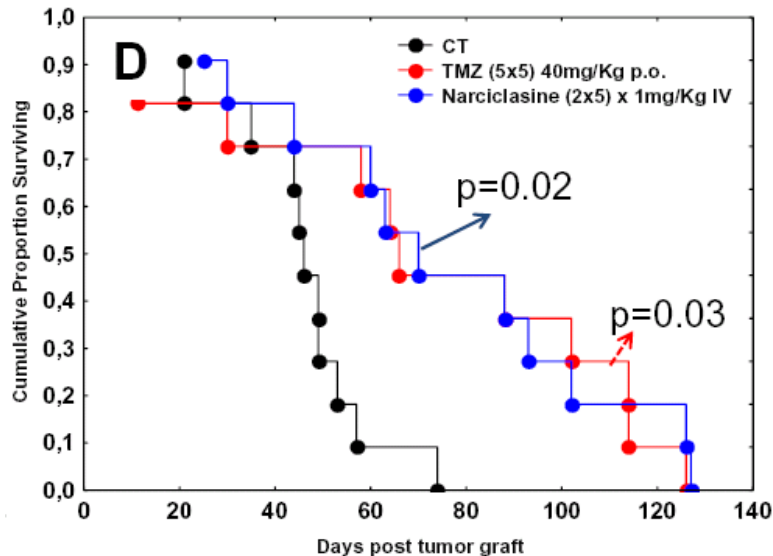
Pline the Old (23-79) used *N. poeticus* and *N. pseudonarcissus* in cancer treatment

Henri de Mondeville (1260-1320) used *Narcissus* in cancer treatment in France



# Narciclasine anti-cancer effects

- Narciclasine is 250X more active on cancer cells than on normal cells
- Narciclasine inhibits protein synthesis which is increased in cancer cells as compared to normal cells. These effects occur at least partly through EF1A inhibition.
- Narciclasine disorganizes the actin cytoskeleton (muscles) of cancer cells
- Narciclasine improves the survival of glioblastoma bearing mice depending on the administration schedule (to be optimized)



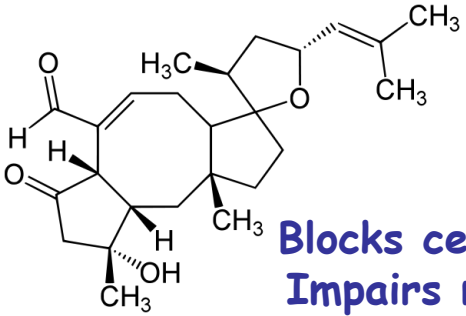
- ➔ Decreases migration
- ➔ Impairs cell division (cytokinesis)

# Drugs from natural sources: other examples

## Fungal phytotoxins



*Helminthosporium oryzae*



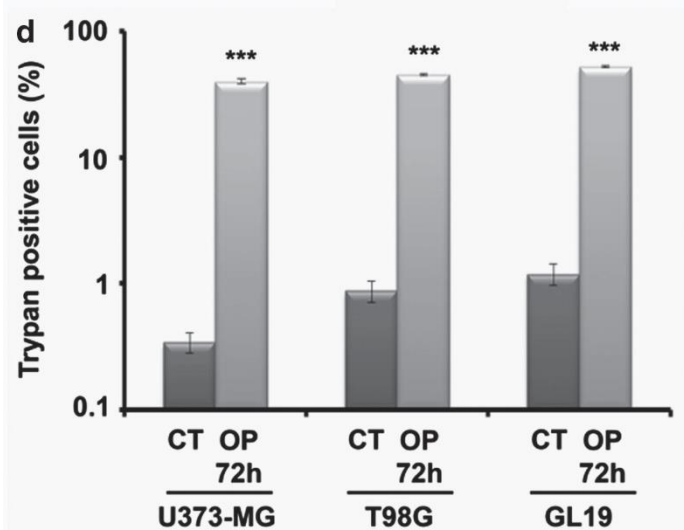
**Ophiobolin A**

**Blocks cell division  
Impairs migration**

Via

**Ion channel targeting**

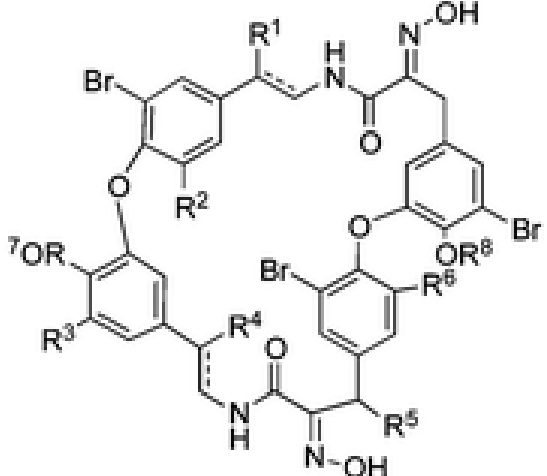
## Glioma cell death



## Compounds from marine sponges



*Ianthella basta*



**Bastadin skeleton**

**Anti-fouling**



**Anti-migratory  
Anti-angiogenic  
Cytostatic or cytotoxic**

# People working on these projects

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- In the laboratory of Toxicology, the following people are working at part or full time on these subject:

- Véronique Mathieu, MD, PhD, ad interim head of the lab
- Robert Kiss, PhD, Director of Research at the « Fonds National de la Recherche Scientifique »
- Marina Bury, PhD student (FRIA granted)
- Laetitia Moreno y Banuls (FNRS granted)
- Thierry Gras (technician)

- These projects are developed also thanks to national and international collaborators: **MANY THANKS TO THEM!!!**

- To see the list, please consult the web page of the laboratory