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National Research Foundation | iThemba LABS
Laboratory for Accelerator Based Sciences

The TUSCC project: What can elephant teach us about cancer prevention and treatment in humans?

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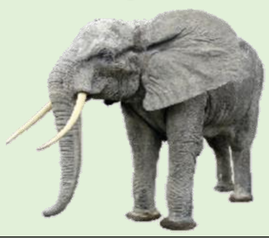
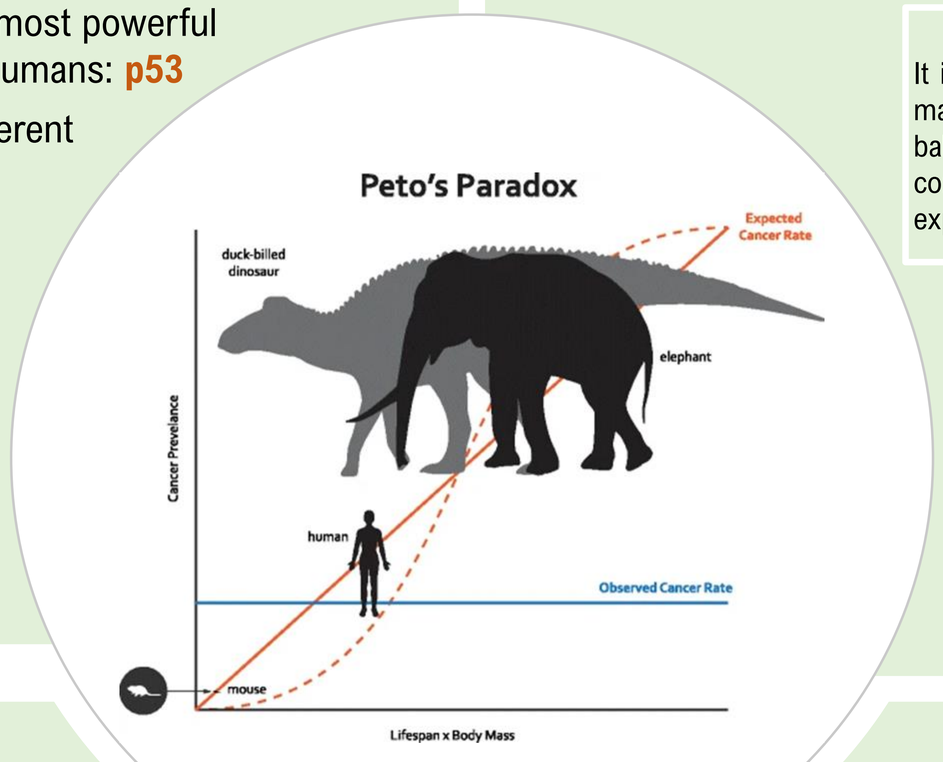
WHY ARE ELEPHANTS CANCER RESISTANT?

- Until 2015, the mechanism was unknown and the answer was discovered in the DNA of an African elephant
- Evolution has fine-tuned elephants to make them cancer resistant, so they harbour dozens of copies of one of the most powerful tumour-suppressor or anti-cancer genes in humans: **p53**
- It is the most frequently mutated gene in different types of human cancers



70 years	Average Life Span	>60 years
65 kg	Average weight	4800 kg
40 billion	Number of cells	40 trillion
25%	Cancer mortality	<5%
1	Copies of p53 gene	20

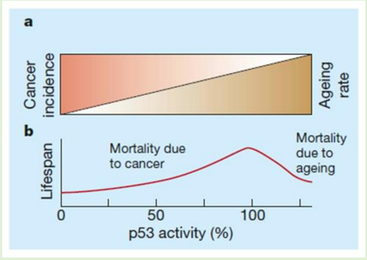


THE GENE DOESN'T COVER THE WHOLE STORY

- Tumour suppression comes with a price. An increase in p53 activity in genetically modified mice, but they aged prematurely and died within a week: **ageing is a side effect of p53 activity**

p53: good cop/bad cop

It is still unclear how elephants manage to maintain a stable balance in p53 function without compromising their long life expectancy!



- An elephant in the Zoo of Naples died of cancer despite the multiple copies of p53
- Elephants in the Zoo are exposed to completely different factors than the African elephants in the wild:

WHAT IS THE ROLE OF ENVIRONMENTAL FACTORS ON CANCER DEVELOPMENT?

STUDY DESIGN

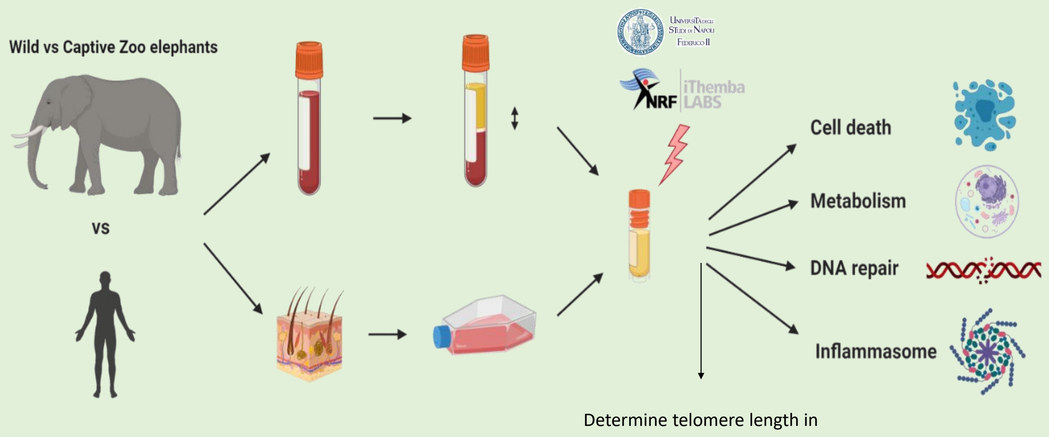
- Only three studies have been conducted up to now, all in the USA, using samples from captive Zoo elephants
- The **stress levels, reproduction, metabolism**… differ between captive and wild elephants. If we want to get to the bottom of the explanation why elephants are more resistant to cancer, we have to take all these factors into account
- What is the impact of ionizing **RADIATION** on the elephant cells?

TUSSC Project: TUmour Suppression and Subdual of Cancer in elephants

1. WORKPLAN

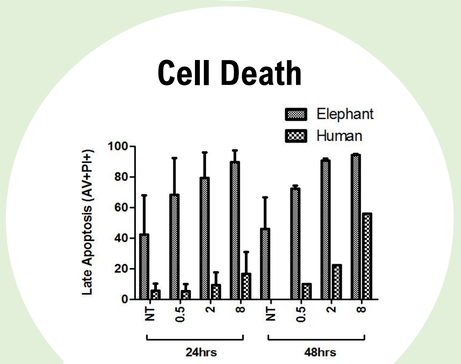
Blood samples collected at Botlierskop (South Africa) and Zoo of Naples (Italy)

Skin samples collected at Botlierskop (South Africa) to establish primary cell cultures



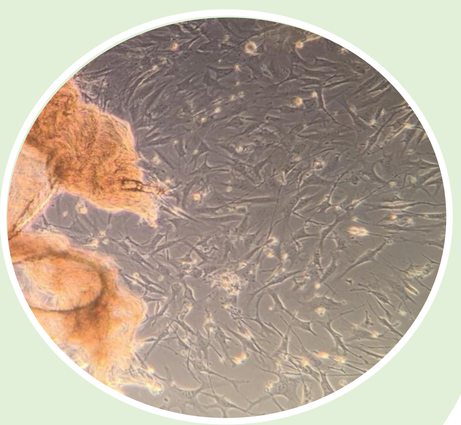
2. FIRST RESULTS

- Blood cells of elephants are very **stress-sensitive** and die rapidly after blood collection.
- No difference in radiation-induced DNA double-strand breaks (DSBs) at 1 h post-irradiation, but less DNA DSBs were observed in elephant cells compared to human cells at 24 h post-irradiation. This confirms that **elephant blood cells repair the induced damage and/or remove damaged cells faster than human blood cells.**
- The **cell death (apoptosis) is higher in elephant blood cells compared to human blood cells** after radiation exposure, even after low doses (0.5 Gy).
  - **How do elephants cope with the high rate of cell loss?**



3. SHORT TERM GOALS

- Several **primary elephant fibroblast cell line have been established in South Africa** from small skin biopsies. This will allow future studies on cell cycle checkpoints, cell survival and chromosomal aberrations
- **Comparative Next Generation Sequencing** of elephant vs human blood cells



4. ULTIMATE GOAL

A BETTER UNDERSTANDING OF THE DIFFERENCES IN DNA DAMAGE RESPONSE BETWEEN HUMANS AND ELEPHANTS AFTER RADIATION EXPOSURE. THE RESULTS WILL CONTRIBUTE TO THE DEVELOPMENT OF NEW CANCER TREATMENTS FOR HUMAN TUMOURS AND THE DESIGN OF NEW STRATEGIES TO PREVENT CANCER DEVELOPMENT

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NATIONAL & INTERNATIONAL PARTNERS:

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