M.A.R.G.E.
Melanoma Apoptosis Reduced Gravity Experiment

APOPTOSIS
Programmed death of cancer cells

IMMUNOTHERAPY

The cell shrinks
Chromatin condenses

Membrane starts blebbing
Organelles disintegrate

Nucleus and organelles collapse
Membrane continues to bleed

Apoptotic bodies form

Macrophages phagocytose apoptotic bodies

Antigens on cell
Signals attract other cells of the immune system

Monoclonal antibody
Monoclonal antibody locked onto antigen

CANCER CELL
MISSION OBJECTIVES

TO PROPOSE AN ALTERNATIVE CURE OF MELANOMA

TO DESIGN A SMALL SCALE CELL CULTURE LABORATORY

TO FOSTER COLLABORATION BETWEEN AEROSPACE AND PHARMACEUTICAL INDUSTRIES
What is Melanoma?

Melanoma is a dangerous skin cancer that begins in cells called **melanocytes**.

It occurs when DNA damage from burning or tanning due to UV radiation triggers mutations in the melanocytes.

**Risk Factors**

- **FAMILY HISTORY**
- **SUN EXPOSURE**
- **FAIR SKIN**
- **FRECKLES AND MOLES**
- **AGE**
The ABCDE rule

**Asymmetry**

**Border**

**Colour**

**Diameter**

**Evolution**

To make it easy for you to check your skin, dermatologist sum up these simple steps to detect skin cancer by observing the moles on the body.
Melanoma Therapy: how do you cure metastasized melanoma?

- Surgical excision
- **Immunotherapy**

**Monoclonal antibodies:**
- Nivolumab (Opvido)
- Vemurafenib (Zelboraf)

In 2018 James Allison and Tasuko Honjo won the **Nobel Prize in Physiology and Medicine** for concluding successfully the study on how the immune system can be used to attack tumoral cells.
Pharmacodynamic

Therapeutic targets

- PD-1 Receptor
- BRAF Mutation
Combined effect of microgravity and immunotherapy

*how could they act together?*

**MICROGRAVITY**

- Decrease focal adhesion
- Decrease invasion capacity
- Inhibition proliferation melanoma cells
- *Apoptosis*

**IMMUNOTHERAPY**

**TUMOR REGRESSION**
Concept

Studying the combined effect of microgravity and immunotherapy on cultures of melanoma cells

**What** should our experimental unit do?  
**How** should it do it?

- **Preserve** melanoma samples, cells culture and drugs
- **Administer** the **drugs** properly
- **Estimate** the **number of cells** and cells growth rate in each sample
- **Ensure** facility **integrity** even if a failure occurs

- **Thermal control system**
- **Hydraulic system**
- **Optical system**
- **Mechanical system**
- **Structures**
ICE Cubes facility

Single-block structure shaped like a 6U CubeSat

Free samples and technical support from “San Gallicano”

Specific installation and positioning requested

4 months in orbit
Space Segment description - optical and mechanical systems

Ratio Nephelometry technique

Improving accuracy by measuring scattered light at different angles

- 45 - 90 - 135 degrees lights and circuit board
- 180 degrees lights and circuit board

- Samples
- OBC and PDU
- Optical system and lights

Spectrometer
Flask
180 degrees lights and circuit board
Space Segment description - optical and mechanical systems

- Aluminum support structure
- Drive belt
- Stepper motor
- Viscoelastic rotary dumper
- Spectrometer rigid base
- Spectrometer belt

- Samples
- OBC and PDU
- Mechanical system
Space Segment description - hydraulic and thermal system

- CO2 Tank
- Culture Tank
- Isolation Panel
- CO2 Electrovalve
- Culture Heating Chamber
- Pumps
- Drug + Culture Heating Chambers
- Aeration Electrovalve
- Drugs Tanks
- Samples
- OBC and PDU
- Hydraulic system
Space Segment description - hydraulic and thermal system

- Heating Chamber
- Heating Wires
- Hydraulic access
- Peltier Coolers
- Thermal Sensor

- Samples
- OBC and PDU
- Hydraulic system
- Thermal system
Pre-Flight

Samples extraction and arrangement in flasks and in the case for launch

Chemical heater and cooler for survival of the samples and culture in the launch phase

Installation:
- launcher: as close as possible to the scheduled launch time
- facility: immediate upon arrival on ISS

Post-Flight

Studying the combined effect of immunotherapy and microgravity on the samples

Compare the ISS results with the ground analysis

Coordinate with ICE Cubes to retrieve the samples
Cycle of operation

- 0:00:00: 
  - Mechanical System, Optical System

- 0:01:00: 
  - Thermal System, Hydraulic System

- 0:02:00:

- 0:03:00:

- 0:04:00:

- 0:05:00:

- 0:06:00:

The cycle of operation operates on a 2-minute cycle, with each interval dedicated to a specific system.
Mass budget

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>MASS [gr]</th>
</tr>
</thead>
<tbody>
<tr>
<td>On Board Computer</td>
<td>135</td>
</tr>
<tr>
<td>Biological System</td>
<td>5195,3</td>
</tr>
<tr>
<td>Thermal System</td>
<td>160,9</td>
</tr>
<tr>
<td>Hydraulic System</td>
<td>2278,9</td>
</tr>
<tr>
<td>Optical System</td>
<td>80</td>
</tr>
<tr>
<td>Mechanical System</td>
<td>293</td>
</tr>
<tr>
<td>TOTAL</td>
<td>8143,1</td>
</tr>
</tbody>
</table>

Power budget

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>PEAK POWER [W]</th>
<th>ENERGY CONSUMPTION [Wh]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Collection Cycle</strong></td>
<td>27,653</td>
<td>/</td>
</tr>
<tr>
<td>(On Board Computer, sensor, electric heater, Optical System, Mechanical System)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sample Maintenance Cycle</strong></td>
<td>22,954</td>
<td>/</td>
</tr>
<tr>
<td>(On Board Computer, sensor, electric heater, Thermal System, Hydraulic System)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ventilation and Air Conditioning</strong></td>
<td>34,454</td>
<td>/</td>
</tr>
<tr>
<td>(Ventilation Valve, CO₂ Valve, Peltier cooler)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>34,5051</strong></td>
</tr>
</tbody>
</table>
### Preliminary risk register

<table>
<thead>
<tr>
<th>Risk and Consequence</th>
<th>P</th>
<th>S</th>
<th>P x S</th>
<th>Mitigation Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malfunction of the hydraulic system, cells do not hire medicinal neither nutrition.</td>
<td>B</td>
<td>4</td>
<td>Low</td>
<td>More detailed tests will be performed on the Hydraulic system in order to prevent the failure of the subsystem.</td>
</tr>
<tr>
<td>Malfunction of the heating system, thermal sensor breakdown.</td>
<td>B</td>
<td>4</td>
<td>Low</td>
<td>More tests will be performed on the Heating system in order to prevent the failure of the subsystem.</td>
</tr>
<tr>
<td>Malfunction of the optical system: Camera breakdown and/or failure of turbidimetry analysis system</td>
<td>A</td>
<td>1</td>
<td>Very Low</td>
<td>Tests will be performed on the optical subsystem to guarantee the correct functioning in order to prevent loss of preliminary data during operations.</td>
</tr>
<tr>
<td>The MARGE project team fails to obtain mission authorization and qualification of the payload</td>
<td>A</td>
<td>4</td>
<td>Very Low</td>
<td>Upon launch, the team will be coordinated by personnel with experience on acquiring legal authorization and qualification for ISS launches.</td>
</tr>
<tr>
<td>Load Factor during the launch leads cell damage</td>
<td>A</td>
<td>4</td>
<td>Very Low</td>
<td>It can lead to several cell membrane damages. Tests will be performed in order to esteem the lower risk of damaging cell membrane possible, in accordance to the load factor of the launch.</td>
</tr>
<tr>
<td>Delay in components procurement and insufficient funding for mission development</td>
<td>B</td>
<td>4</td>
<td>Low</td>
<td>Several funding sources are taken into account during the preliminary phase of the project and procurement phase will be started in time in order to prevent delays.</td>
</tr>
<tr>
<td>Load Factor leads to experiment break up</td>
<td>A</td>
<td>5</td>
<td>Medium</td>
<td>Experiment structure will be over-tested in order to reduce probability of damages or break ups during launch.</td>
</tr>
</tbody>
</table>
Implementation plan

Project Planning
- 2 years

Procurement
- 6 months

Design
- 8 months

Subsystem development
- 2 months
- Structure
- OBDH
- EPS
- TT&C
- Biological Payload

Testing Phase
- 2 months

Launcher integration

Software preparation
- 10 months

Experimental Operation
- 4 months

Data analysis
- 9 months

Milestones

End of data analysis

Start of Operations
Launch
Delivery of the experiment
Kick-off of the project
Conclusion

It has been proven that microgravity can induce apoptosis.

Interest in studying the combined effect of microgravity and monoclonal drugs on melanoma.

Autonomous system allocated in a 6U CubeSat.

Monitoring of the samples during the in orbit time made by a turbidimetric analysis.

Post analysis of the expected effects of microgravity after the 4 months of operational phase.
Thank you for your attention!
Combined effect of microgravity and immunotherapy

- Apoptosis
- Inhibition proliferation of melanoma cells
- Loss of function mTORC1
- Structural alteration of Cytoskeleton

- Decrease of focal adhesions
- Decrease of invasion capacity
- Inhibition of MMP9
M.A.R.G.E

Autonomous laboratory

Mechanical System

Thermal System

Hydraulic System

Optical System

ISS experiment in a 6U IceCube Facility

6 Melanoma samples

Effects of microgravity and monoclonal drugs

Turbidimetry analysis
# Mass budget

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>COMPONENT</th>
<th>MASS [kg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal System</td>
<td>Thermal Sensor (x11) (TMP36)</td>
<td>0.1320</td>
</tr>
<tr>
<td></td>
<td>Electric Heaters</td>
<td>0.0099</td>
</tr>
<tr>
<td></td>
<td>Peltier Cell (x2)</td>
<td>0.0230</td>
</tr>
<tr>
<td></td>
<td>Pumps (x5)</td>
<td>0.0750</td>
</tr>
<tr>
<td></td>
<td>Electric Valve for CO₂</td>
<td>0.0900</td>
</tr>
<tr>
<td></td>
<td>Culture Aluminum Tank</td>
<td>1.4236</td>
</tr>
<tr>
<td></td>
<td>CO₂ Aluminum Tank</td>
<td>0.5421</td>
</tr>
<tr>
<td></td>
<td>Drug Tanks Aluminum</td>
<td>0.0461</td>
</tr>
<tr>
<td></td>
<td>Heat Chamber Aluminum</td>
<td>0.0812</td>
</tr>
<tr>
<td></td>
<td>Tubes</td>
<td>0.0200</td>
</tr>
<tr>
<td></td>
<td>Raspberry Pi 4 B</td>
<td>0.0700</td>
</tr>
<tr>
<td></td>
<td>Driver</td>
<td>0.0650</td>
</tr>
<tr>
<td>OBC</td>
<td>Melanoma Samples</td>
<td>0.1200</td>
</tr>
<tr>
<td></td>
<td>Culture Medium</td>
<td>4.830</td>
</tr>
<tr>
<td></td>
<td>Nivolumab</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>Venurafenib</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>CO₂</td>
<td>0.0342</td>
</tr>
<tr>
<td>Biological System</td>
<td>Sample Flask (x6)</td>
<td>0.2411</td>
</tr>
<tr>
<td></td>
<td>PCS Light 180</td>
<td>0.0100</td>
</tr>
<tr>
<td></td>
<td>PCS Light 45/90/135</td>
<td>0.0300</td>
</tr>
<tr>
<td>Optical System</td>
<td>Spectrometer</td>
<td>0.0400</td>
</tr>
<tr>
<td></td>
<td>Camera Engine (Stepper Motor NEMA 14)</td>
<td>0.1800</td>
</tr>
<tr>
<td></td>
<td>Viscoelastic rotary Damper</td>
<td>0.0120</td>
</tr>
<tr>
<td></td>
<td>Transmission Belt</td>
<td>0.0007</td>
</tr>
<tr>
<td></td>
<td>Sensor Belt</td>
<td>0.0659</td>
</tr>
<tr>
<td></td>
<td>Support structure and Sensor base</td>
<td>0.0313</td>
</tr>
<tr>
<td></td>
<td>Heat Insulator (Dopron)</td>
<td>0.0031</td>
</tr>
<tr>
<td>Mechanical System</td>
<td>TOTAL</td>
<td>8.1431</td>
</tr>
</tbody>
</table>
# Power budget

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensor (x11)</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td>1.928*10^3</td>
<td></td>
</tr>
<tr>
<td>Electric Heater</td>
<td>2.652</td>
<td>2.652</td>
<td>2.652</td>
<td>2.652</td>
<td>2.652</td>
<td>2.652</td>
<td>2.652</td>
<td>2.6524</td>
</tr>
<tr>
<td>Heat Chamber (X3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.3</td>
<td></td>
<td>0.0024</td>
</tr>
<tr>
<td>Peltier Cooler (x2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.8</td>
<td></td>
<td>16.62</td>
</tr>
<tr>
<td>SBC (Single Board Computer)</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td></td>
</tr>
<tr>
<td>Culture and Waste Pumps (x3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6</td>
<td></td>
<td>7.5*10^4</td>
</tr>
<tr>
<td>Drug Pumps (x2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.4</td>
<td></td>
<td>4*10^6</td>
</tr>
<tr>
<td>Air Pump</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.2</td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>Electric CO₂ Valve</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.8</td>
<td></td>
<td>0.0044</td>
</tr>
<tr>
<td>Spectrometer and Lighting</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camera Engine</td>
<td>3.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0379</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>POWER USED</strong></td>
<td>27.653</td>
<td>21.554</td>
<td>22.954</td>
<td>18.654</td>
<td>22.454</td>
<td>34.454</td>
<td>17.854</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL ENERGY CONSUMPTION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5051.</td>
</tr>
</tbody>
</table>