INTERNATIONAL ATOMIC ENERGY AGENCY
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INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
34100 TRIESTE (ITALY) - P.O.B. 586 - MIRAMARE - STRADA COSTIERA 11 - TELEPHONE: 2240-1
CABLE: CENTRATOM - TELEX 460392-I

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WORKSHOP ON SPACE PHYSICS:
"Materials in Micorgravity"
27 February - 17 March 1989

"The Role of Gravity in Cellular Events"

A. COGOLI
Space Biology Group
Institute of Biotechnology
ETH-Höggerberg
Zurich, Switzerland

Please note: These are preliminary notes intended for internal distribution only.

WORKSHOP ON
SPACE PHYSICS
MATERIALS IN MICROGRAVITY
TRIESTE FEBRUARY 27 - MARCH 17 1989

THE ROLE OF GRAVITY IN CELLULAR EVENTS

AUGUSTO COGOLI
SPACE BIOLOGY GROUP
INSTITUTE OF BIOTECHNOLOGY
ETH-HÖNGGERBERG
ZÜRICH

BASIC QUESTIONS

- ARE BIOLOGICAL SYSTEMS (CELLS) SENSING GRAVITY?
- IF YES, HOW?
  - * G-RECEPTORS?

OBJECTIVES

- BASIC RESEARCH
- BIOMEDICINE
- BIOTECHNOLOGY

IMPORTANT ENVIRONMENTAL PARAMETERS

- MICROGRAVITY
- COSMIC RADIATION

SYTEMS FOR BIOLOGICAL EXPERIMENTS IN MICROGRAVITY

ORBITAL SYSTEMS:		
- AUTOMATIC SATELLITES:		
* BIOSATELLITE	(U.S.A.)	2-3 D
* BIOCOSMOS	(U.S.S.R.)	7-28 D
- MANNED STATIONS AND LABORATORIES:		
* SKYLAB	(U.S.A.)	30-90 D
* SPACELAB	(EUROPE)	7-10 D
* SALYUT	(U.R.R.S.)	≤ 180 D
* MIR	"	> 1 A
SUB-ORBITAL SYSTEMS:		
* SOUNDING ROCKETS		7-10 MIN
STRATOSPHERIC BALLOONS:		
* FREE-FALL PAYLOADS		3 MIN
PARABOLIC FLIGHTS:		15-35 S
FALL TOWER:		4 S
EUROTUB:		30 S
LABORATORY SIMULATORS:		
* FAST ROTATING CLINOSTAT		UNLIMITED
* FREE-FALL MACHINE		"

BIOLOGICAL AND PHYSICAL ASPECTS OF SINGLE CELL CULTURES IN MICROGRAVITY

WITHIN THE CELL

* SEDIMENTATION / DISTRIBUTION OF CELL ORGANELLES
* CYTOPLASMIC STREAMING / DISTRIBUTION OF NUTRIENTS AND WASTE PRODUCTS
* CELL SHAPE / MEMBRANE FUNCTION
* CELL MOVEMENTS / CELL-CELL INTERACTIONS

DISTINGUISH BETWEEN

* ADHERING / NON-ADHERING CELLS
* DIFFERENTIATING / NON-DIFFERENTIATING CELLS
* AMEBOIDAL MOVEMENTS / ACTIVE SWIMMING
* RECEPTION / SENSITIVITY

PHYSICAL EFFECTS

* THERMAL CONVECTION / THERMOSOLUTAL CONVECTION
* DIFFUSION
* GAS- / LIQUID- PHASE INTERFACE
* MICROGRAVITY / COSMIC IRRADIATION

ALTERATION OF CELLULAR FUNCTIONS IN MICROGRAVITY

CELL TYPE	FUNCTION ALTERED
HUMAN EMBRYONIC LUNG CELLS	20% REDUCTION OF GLUCOSE CONSUMPTION
HUMAN LYMPHOCYTES	500% INCREASE OF INTERFERON BIOSYNTHESIS 90% INHIBITION OF MITOGENIC ACTIVATION
PARAMECIUM AURELIA	100% INCREASE OF GROWTH RATE
ESCHERICHIA COLI	40% INCREASE OF CONJUGATION 300% RESISTANCE TO ANTIBIOTICS
CLAMYDOMONAS BACILLUS SUBTILIS ANISE CELLS	MANYFOLD INCREASE OF BIOMASS YIELD
PHYSARUM POLYCEPHALUM	INCREASE OF FREQUENCY AND VELOCITY OF CYTOPLASMIC MOVEMENTS

Table 1. Effects of spaceflight on single cells organisms, plant and mammalian cells, from Gmünder and Cogoli

Bacteria			
Organism	Qualitative effects	Quantitative effects	Mission (Duration of the experiments)
Escherichia coli	Slight increase of phage productivity, and slightly higher survival rates of bacteria.		Vostok 4 & 6 (27-30 h) Zond 5 & 7 (?)
Salmonella typhimurium	Increased resistance against high doses of radiation.	In stationary phase, mean total cell density was increased by 15%. This increase was due to vibration and acceleration. However, mean viable density was increased by 30%. Vibration and acceleration alone contributed only to an increase of 8%.	Biosatellite II (2 d)
Escherichia coli	Increased resistance against high doses of radiation. Final viable cell density slightly increased.		Biosatellite II (2 d)
Proteus vulgaris		Final cell number 7 times higher.	Soyus 12 (2 d)
Staphylococcus aureus		Minimal inhibitory concentrations of oxacillin, chloramphenicol and erythromycin increased up to 2 times.	Salyut 7 (1 d)
Escherichia coli		Minimal inhibitory concentrations of colistin and kanamycin 2-4 times higher. Other factors than microgravity affect this behavior.	Salyut 7 (1 d) D-1 (1 d)
Bacillus subtilis	Higher yield of biomass. (inflight photometer went out of range)	5×10^4/ml spores recovered in the flown sample and 8×10^5/ml spores in the control, respectively. In space, the cells were found to be lysed in the stationary phase, whereas 3×10^7/ml cells were found in the control.	D-1 (3 d)
Escherichia coli		No effects of spaceflight on transduction and transformation. Conjugation enhanced under microgravity by up to 40%.	D-1 (3 h)
Slime molds			
Physarum polycephalum	Reduced myxomycetous growth.	Protoplasmic movement (migration index) was significantly reduced by 37-53% postflight.	Cosmos 1129 (?)
Physarum polycephalum	Acceleration stimuli influenced the regulation of mobility (contraction rhythmicity). Period of contraction/relaxation cycles decreased.		D-1 (20-90 min)
Algae and plant cells			
Chlorella sp.	No effect of spaceflight on growth characteristics. Viability, growth rate, proportion of photosynthetically active cells and mutation rate were not affected. However, a decrease of chloroplast volume and other slight ultrastructural changes were reported. Some earlier findings are contradicting.		Soyuz 12, Cosmos 573 (up to 10 d)
Chlamydomonas sp.		Circadian rhythmus (period and phase) of photoaccumulation behavior did not change significantly in both strains tested. However, the amplitude was more pronounced (2.9 times for wild type-strain (wt), 3.7 times for short period strain (s)). Survival rates were 1.95-fold and 1.66-fold higher (wt and s, respectively). The proliferation rate was 100% and 50% higher in space in the wt and s, respectively.	D-1 (6 d)

Table 1. continued

Algae and plant cells			
Organism	Qualitative effects	Quantitative effects	Mission (Duration of the experiments)
Anise cell suspension	Evidence of enhanced biomass production.		D-1 (7 d)
Euglena, Nostoc	Long term survival of system (only preliminary results available at present).		Long March II (4.5 d)
Protozoa			
Pelomyxa carolinensis	A trend toward higher division rates in well fed Pelomyxae was noted in space.		Biosatellite II (2 d)
Pelomyxa carolinensis	No effect of spaceflight on survival and growth rate and physiological, morphological and cytochemical parameter.		Biosatellite II (2 d)
Paramecium tetraurelia	Inflight cells were larger during early log phase but smaller at later growth stages. Cells showed a tendency to be more spherical under microgravity. Cell protein, Mg, Ca contents were decreased.	Growth rate in microgravity 1.93 times higher. Yield after 5 days was 3.7 times elevated (results from D-1 mission, result from Cytos experiment are less pronounced).	Salyut 6 (4 d) D-1 (5 d)
Mammalian cells			
Human tumor cells (HeLa)	Slight increase in cell size. Trend to higher viability.		Zond 5 & 7 (?)
Human embryonic lung cells (WI 38)	No effect of spaceflight on lag-phase, growth rate, and a variety of morphological parameters.	Cells consumed 20% less glucose. No other significant differences.	Skylab III (28 d)
Human lymphocytes		Interferon secretion using various inducers 5 times increased.	Salyut-6 (4-6 d)
Chinese hamster cells	Macroscopic inspection: no change. Microscopic: fewer but larger microcolonies and many spheriod cells were found. Differences observed in cellular ultrastructure (electron microscopy).		Salyut-6 (6 d)
Human kidney cells	No effect of spaceflight on attachment and morphology.		STS-8 (1 d)
Human kidney cells	No effect of spaceflight on morphology of quiescent cells.		STS-8 (5 d)
Human lymphocytes	Reduced lymphocyte aggregation in microgravity. However, cluster formation of monocyte like cells was noted.	Mitogen induced activation in microgravity reduced by more than 90%.	Spacelab-1 (3 d) D-1 (4 d)
Hybridoma cells	Morphological results not yet available.	No effect of spaceflight on growth rate. Viability in microgravity was slightly reduced by 15%.	D-1 (6 d)
Human red blood cells	Normal blood showed roulaux formation on ground, but a random swarm like pattern in space. Cells from patients (various diseases) formed roulaux in space, whereas severe clumping was observed in the controls.		STS 51-C (3 d)

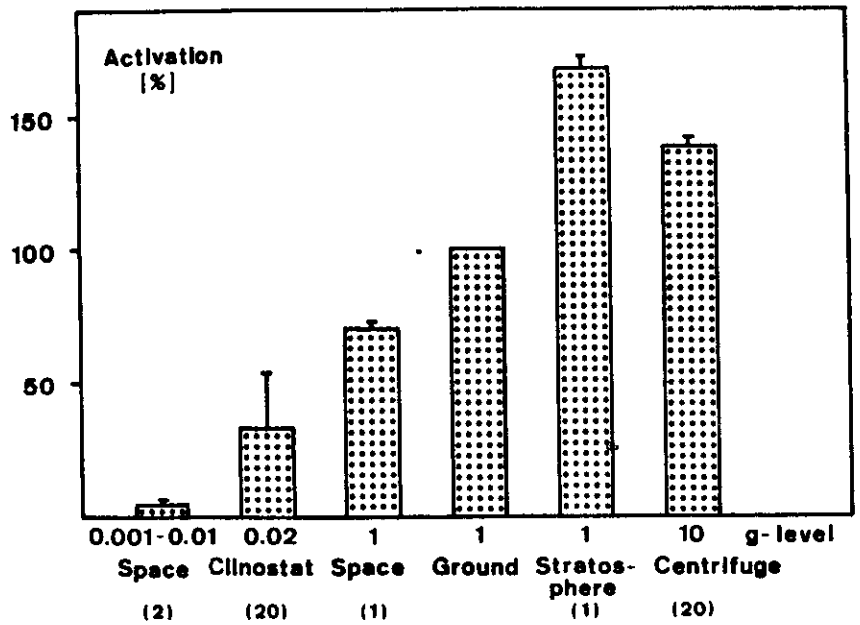

Fig. 1. Summary of gravitation and cosmic radiation effects on lymphocytes. The results are expressed as percent of the corresponding 1xg controls. The numbers of experiments performed are given in parenthesis.

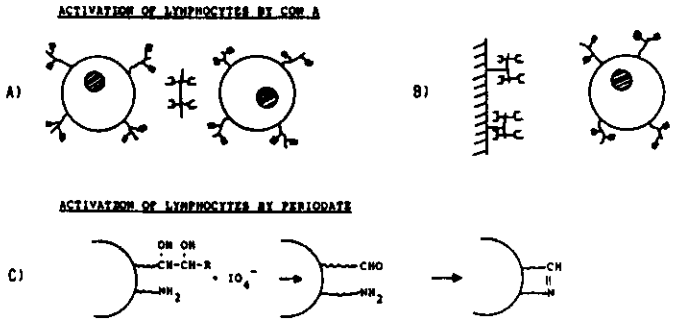

Fig. 2 PATHWAYS OF ACTIVATION OF LYMPHOCYTES IN VITRO

A: T-lymphocytes are activated by Con A dissolved in the medium,
B: B-lymphocytes are activated by Con A bound to a substrate,
C: T-lymphocytes are activated after oxidation of sugar residues with sodium periodate (30 min at 0 °C).

EQUIPMENT REQUIRED FOR CELL CULTIVATION IN SPACE

- INCUBATORS
- REFERENCE CENTRIFUGES
- AUTOMATED TRANSFER OF FLUIDS
- MICROSCOPES
- VIDEORECORDING DEVICES
- STORAGE: FREEZERS / REFRIGERATORS
- BIOREACTORS
- REFERENCE CENTRIFUGES
- BIOCOMPATIBLE CELL CULTIVATION CONTAINERS
- TELESCIENCE

BIOTECHNOLOGY (OR BIOPROCESSING) COMPREHENDS PROCESSES

BY WHICH LIVING CELLS OR CELLULAR EXTRACTS

ARE USED FOR THE PRODUCTION OF

USEFUL AND COMMERCIALLY RELEVANT SUBSTANCES

EXAMPLES:

- FERMENTATION
- GENETIC ENGINEERING
- HYBRIDOMA TECHNOLOGY
- CELL CULTIVATION

FOR THE PRODUCTION OF:

- PENICILLIN
- VACCINES
- MONOCLONAL ANTIBODIES
- GROWTH HORMONES

A BIOTECHNOLOGICAL PROCESS BASED ON CELLULAR FUNCTIONS OR STRUCTURES WHICH ARE ALTERED IN MICROGRAVITY IS LIKELY TO BE ALTERED AS WELL

ETH Eidgenössische Technische Hochschule Zürich
Ecole polytechnique fédérale de Zurich
Politecnico federale di Zurigo
Swiss Federal Institute of Technology Zurich

A. Cogoli