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Surname		Other name	s
Pearson Edexcel International Advanced Level	Centre Number		Candidate Number
Biology International Advar Unit 5: Respiration, Coordination and G	Internal Er		ment,
Sample Assessment Materials for firs Time: 1 hour 45 minutes	t teaching Septem	ber 2018	Paper Reference WBI15/01
You must have: Scientific article (enclosed), scie		1 110	Total Marks

Instructions

- Use **black** ink or **black** ball-point pen.
- **Fill in the boxes** at the top of this page with your name, centre number and candidate number.
- Answer **all** questions.
- Answer the questions in the spaces provided
 there may be more space than you need.
- Show all your working in calculations and include units where appropriate.

Information

- The total mark for this paper is 90.
- The marks for each question are shown in brackets
 use this as a guide as to how much time to spend on each question.
- In questions marked with an asterisk (*), marks will be awarded for your ability to structure your answer logically, showing how the points that you make are related or follow on from each other where appropriate.

Advice

- Read each question carefully before you start to answer it.
- Try to answer every question.
- Check your answers if you have time at the end.

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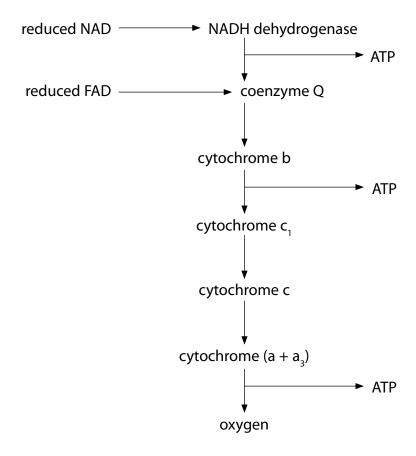


Answer ALL questions.

Write your answers in the spaces provided.

Some questions must be answered with a cross in a box \boxtimes . If you change your mind about an answer, put a line through the box \boxtimes and then mark your new answer with a cross \boxtimes .

1 The diagram shows the sequence of electron carriers in the electron transport chain. The diagram also shows the stages where ATP is generated.



(a) Where is the site of the electron transport chain?

(1)

- A cytoplasm
- B inner mitochondrial membrane
- C matrix
- **D** outer mitochondrial membrane

(b)	The table gives	some information	n about inhibito	ors of the electron	transport chain.
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Inhibitor	Site of inhibition
Cyanide	between cytochrome (a + a_3) and oxygen
Rotenone	between NADH dehydrogenase and coenzyme Q

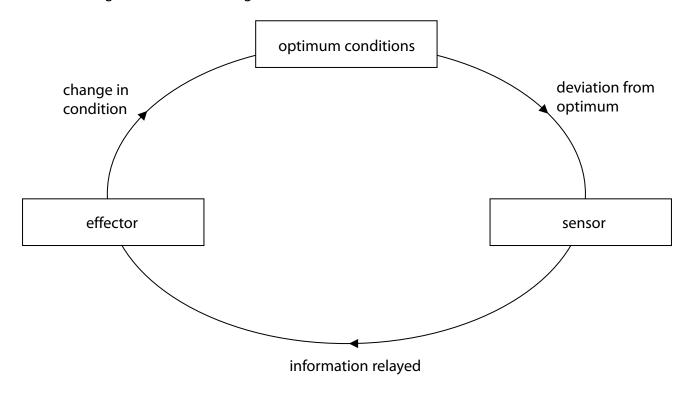
transport chain.	(2)
	(-,
(ii) Metabolism of succinate results in the produc	tion of reduced FAD.
Explain the effect that rotenone will have on	ATP production by the electron
transport chain.	(2)
	(2)

(iii) Explain why these inhibitors will not affect the production of ATP from anaerobic respiration. Use the information in the table to support your answer	. (2)
(Total for Question 1 = 7 ma	rks)

2 (a) Negative feedback is important in maintaining homeostasis.

Control of the ventilation rate is an example of negative feedback.

The diagram summarises negative feedback.



(i) Which row of the table shows the sensor and the location of the sensor involved in the control of ventilation?

(1)

	sensor	location of sensor
⊠ A	baroreceptor	hypothalamus
В	baroreceptor	medulla oblongata
	chemoreceptor	hypothalamus
⊠ D	chemoreceptor	medulla oblongata

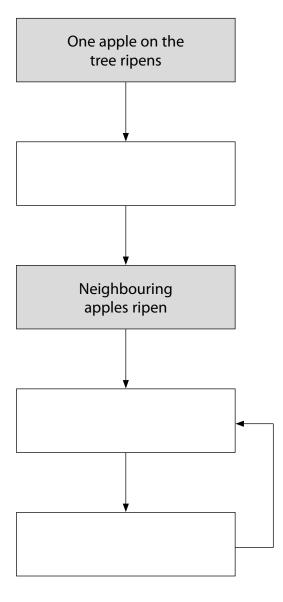
(ii) Explain why the control of ventilation rate is an example of negative feed Use the information in the diagram to support your answer.	
	(4)

(b) The ripening of apples is an example of positive feedback.

Ethene is a gas that causes apples to ripen. Ripe apples release ethene.

Complete the diagram to show positive feedback in the ripening of apples.

(3)



(Total for Question 2 = 8 marks)

3 A number of insects can transmit disease when they bite their hosts.

The photograph shows *Rhodnius prolixus*, a blood-sucking insect that transmits Chagas disease between humans.

This insect feeds on blood by extending its proboscis and pushing it through the skin of a person. It is thought to do this when it detects body warmth.



© Oxford Scientific/Getty Images

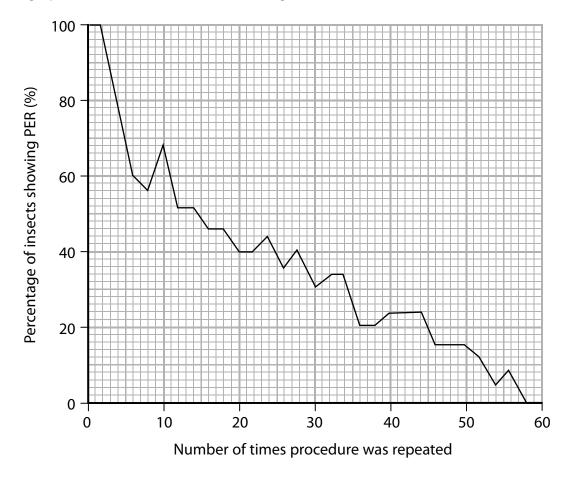
An investigation was carried out to study the effect of a heat stimulus on the proboscis extension response (PER).

Insects were kept in a temperature-controlled container with a heat pad placed in front of them. The heat pad could be touched by the proboscis when fully extended.

The heat pad was initially set at $25\,^{\circ}$ C. It was then heated up to $35\,^{\circ}$ C and the number of insects with a fully-extended proboscis were counted. It was then returned to a temperature of $25\,^{\circ}$ C.

This procedure was repeated a number of times.

The graph shows the results of this investigation.



(a) In this investigation, 350 insects were used.

Calculate the mean decrease in the number of insects showing PER each time the procedure was repeated.

(3)

Answer

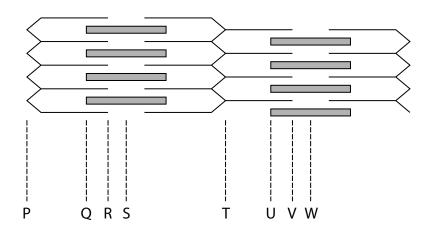
e) Explain the results of this investigation.	(3)
) Suggest why a drop in PER to a heat stimulus could be an advantage to these insects.	(2)
	(=)

- **4** Movement in mammals results from the interaction between muscles, tendons, ligaments and the skeleton.
 - (a) Which row of the table describes tendons and ligaments?

(1)

	Tendons	Ligaments
⊠ A	flexible, non-elastic tissue connecting bone to bone	flexible tissue connecting muscle to bone
⊠ B	flexible, non-elastic tissue connecting muscle to bone	flexible tissue connecting bone to bone
⊠ C	flexible tissue connecting bone to bone	flexible, non-elastic tissue connecting muscle to bone
⊠ D	flexible tissue connecting muscle to bone	flexible, non-elastic tissue connecting bone to bone

(b) (i) The diagram shows part of a skeletal muscle fibre.



Which pair of letters represents one sarcomere?

(1)

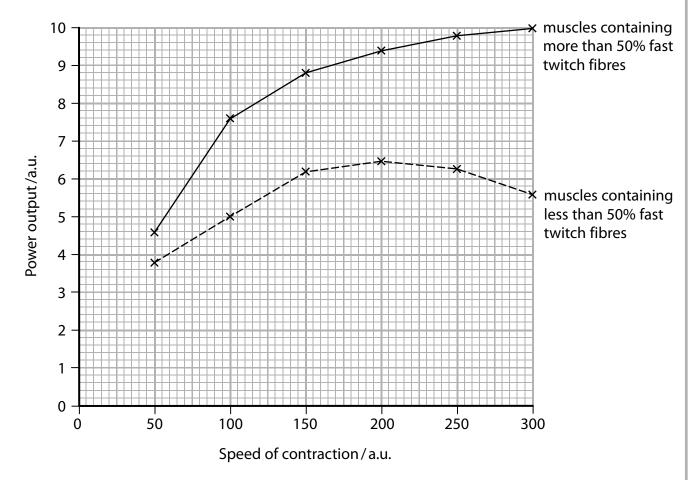
- A PtoT
- ☑ B Q to U
- C R to V
- ☑ D S to W

(ii) Compare and contrast the structure of fast-twitch and slow-twitch muscle fibres.	
	(4)

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*(c) The power output of a muscle depends on the speed of contraction and the proportion of fast-twitch and slow-twitch fibres in the muscle.

The graph shows the relationship between the power output and the speed of contraction of two different types of muscle.



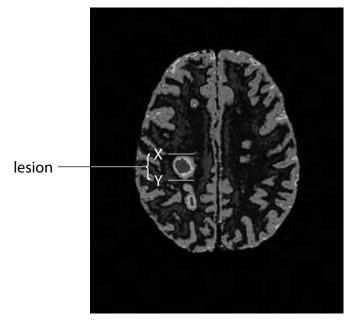
knowledge to support your answer.			(6)
			(6)
	(Tot	al for Question 4	– 12 marks)
	(100	<u></u>	_ 12 mana,

5 Multiple sclerosis (MS) is a disease that causes the destruction of the myelin sheaths around neurones.

This destruction is caused by the person's own immune system.

Lesions form in the brain where myelin is destroyed.

(a) The photograph shows lesions in the brain of a person with MS, as seen using magnetic resonance imaging (MRI).



© M210/0087 SGI/Science Photo Library

The actual length of this brain is 15 cm.

Calculate the actual diameter, in mm, of the lesion between X and Y.

(2)

Answer mm

(b) The table shows the speed of conduction of an impulse along non-myelinated and myelinated neurones with axons of different diameters.

Type of neurone	Diameter of axon / μm	Speed of conduction of impulse / m s ⁻¹
non-myelinated	1	2.3
non-myelinated	2	3.1
non-myelinated	4	4.2
myelinated	1	2.6
myelinated	2	8.5

six times greater in a myelinated neurone than in a non-myelinated neurone.	
	(2)

(i) Show that the effect of diameter on the speed of conduction of an impulse is

speed of conduction of an impulse.	(4)
(iii) Symptoms of MS can include blindness in one eye and lack of coordi	nation.
Suggest why a person with MS could have these symptoms.	(3)

The ki	dne	y is involved in osmoregulation and the production of urine.	
		hich substances are filtered from the blood in the renal capsule?	
X		glucose and fibrinogen	(1)
X	В	glucose, fibrinogen and urea	
X	C	glucose and urea	
X		urea and prothrombin	
		area and prounomon	
(ii)	Wl	hich structure is acting as the filter in the renal capsule?	(1)
\times	A	basement membrane	(-)
\times	В	cells lining the renal capsule	
\times	C	endothelial cells in the walls of the capillaries	
\times	D	podocytes	
	ce	hich transport mechanism is responsible for the uptake of glucose into the lls of the wall of the proximal tubule?	(1)
×	A	diffusion	
\boxtimes	В	endocytosis	
X		sodium co-transport	
X	U	osmosis	
(iv) Ex	plain why some urea is reabsorbed in the proximal tubule.	(2)
			(2)

(b) In an investigation, salt solution was injected into the carotid artery of a mammal. The carotid artery carries blood to the head.

The rate of urine production was measured after the injection.

The table shows the results.

Time after injection of salt solution / min	Rate of urine production / cm³ min-1
0	7.0
5	1.1
10	0.6
15	1.0
20	1.5
25	2.2
30	2.4

(i) Calculate the percentage decrease in the rate of urine production 10 minutes after the injection.

Give your answer to 2 decimal places.

(2)

Answer%

- (ii) At what times should more measurements be taken to find the lowest rate of urine production?
- (1)

- **A** at 1-minute intervals between 5 minutes and 10 minutes
- **B** at 1-minute intervals between 5 minutes and 15 minutes
- ☑ C at 1-minute intervals between 10 minutes and 15 minutes.
- **D** at 5 minutes, 10 minutes and 15 minutes, two more times

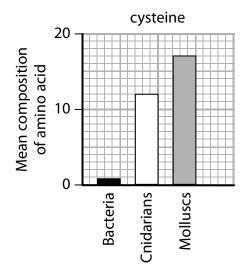
(iii) Explain the results of this investigation. Use the information in the table to support your answer.	(4)
(Total for Question 6 = 12 r	marks)

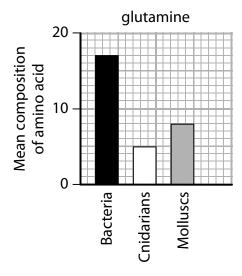
7	Soi	me	groups of living organisms produce neurotoxins.	
	Ne	uro	toxins act at synapses, preventing the generation of nerve impulses.	
			scientists have been studying neurotoxins using a combination of uter science, statistics and mathematics.	
	(a)		nat is the name of a study that combines computer science, statistics and athematics?	(4)
	X	A	bioinformatics	(1)
	X	В	computed tomography	
	X	C	epigenetics	
	X	D	forensic entomology	
	(b)	So	me neurotoxins act in these ways:	
		•	inhibiting the release of acetylcholine	
		•	blocking of ion channels	
		•	blocking of acetylcholine receptors.	
		Ex	plain how these neurotoxins prevent the generation of nerve impulses.	(3)

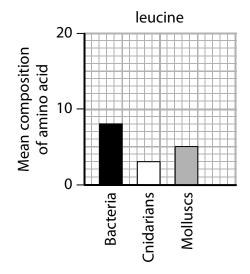
(c) The table shows the mean composition of three amino acids, in neurotoxins and non-toxins.

Type of amino acid	Mean composition of amino acid in neurotoxins	Mean composition of amino acid in non-toxins
Cysteine	13.69	1.95
Glutamine	2.35	4.16
Leucine	5.53	10.17

The graphs show the mean composition of these amino acids in neurotoxins produced by three groups of organisms: bacteria, cnidarians and molluscs.







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information in the table and in the graphs to support your answer.	(6)

(ii) Explain why the replacement of one amino acid in a neurotoxin could decrease its toxicity.	
decrease its toxicity.	(2)
(Total for Question 7 = 12 m	arks)

	8	The scientific document you have studied is adapted from an article in nature.com: Microgravity elicits reproducible alterations in cytoskeletal and metabolic gene and protein expression in space-flown Caenorhabditis elegans. Use the information from the scientific document and your own knowledge to	
l		answer the following questions.	
l		(a) Suggest why the authors of this article have named the species of nematode used in this study (paragraph 2)	
		in this study (paragraph 2).	(1)
		(b) State one ethical issue of using nematodes in this study.	(1)
		(c) Describe how microgravity can cause changes in gene expression in these nematodes (paragraph 4).	(3)

nematodes grow	n in microgravity (paragraph 4).		(3)
e) Explain why ther	e were reduced levels of a number of	metabolic proteins i	n
e) Explain why there nematodes grow	e were reduced levels of a number of nin microgravity (paragraph 6).	metabolic proteins i	n
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(h) Comment on the reliability of the data presented in Table 1 (paragraph 9).	(3)
(Total for Question 8 = 2	0 marks)
TOTAL FOR PAPER = 90) MARKS

Pearson Edexcel International Advanced Level

Biology

Unit 5: Respiration, Internal Environment, Coordination and Gene Technology

Sample Assessment Materials for first teaching September 2018

Paper Reference

Scientific article for use with Question 8

WBI15/01

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Scientific article for use with Question 8

Microgravity elicits reproducible alterations in cytoskeletal and metabolic gene and protein expression in space-flown *Caenorhabditis elegans*

Introduction

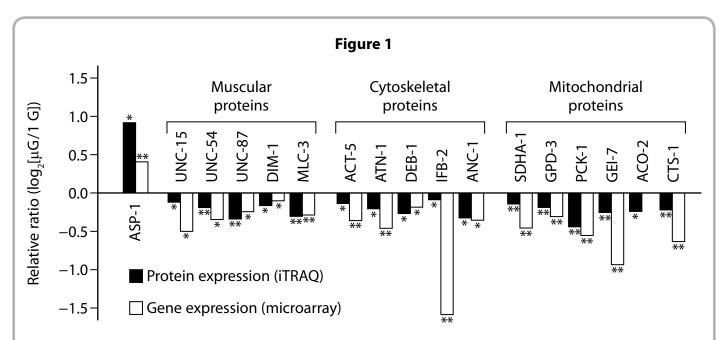
- 1. Spaceflight-induced muscle atrophy poses a significant risk for astronaut health and mission performance. Accordingly, it is a major obstacle for manned deep-space exploration. In contrast to observations on the Earth, exercise countermeasures employed during spaceflight have proven ineffective for maintaining skeletal muscle mass. Although the optimal exercise and nutritional strategies might simply have not yet been developed, there is growing evidence that muscle may be intrinsically sensitive to the effects of spaceflight *per se*. For example, vascular and cardiac muscles undergo atrophy, without reported muscle unloading, and cultured embryonic muscle synthesizes less protein as a direct consequence of spaceflight. However, the molecular events regulating these changes remain unclear.
- 2. Here we aimed to identify the mechanisms that are triggered in response to microgravity using the nematode *Caenorhabditis elegans*. In this space experiment (CERISE; *C. elegans* RNA Interference in Space Experiment), we synchronously cultured L1 larvae-stage animals to adulthood in liquid media for 4 days either in microgravity or 1-G (gravitational acceleration unit) centrifuge conditions onboard the Japanese Experiment Module of the International Space Station (ISS). The nematode larvae were launched to the ISS onboard the Space Shuttle Atlantis STS-129 on 16 November 2009, cultures were initiated on 20 November 2009, and the post-cultivation frozen samples were returned by the Space Shuttle Endeavour STS-130 on 21 February 2010.
- 3. *C. elegans* is an ideal model organism for studies of the physiological effects of space environments because of its small size, short life cycle, and because of its common use on Earth as a model organism for human medical pathologies. The first examinations of the effects of the space environment, including cosmic radiation, on *C. elegans* were performed using essentially standard laboratory culturing techniques with agar plates. *C. elegans* can mate, reproduce, and undergo embryonic development during spaceflight, and radiation-induced mutations can be monitored during spaceflight experiments. During the Dutch Soyuz mission DELTA to the ISS in April 2004, an international collaboration of laboratories carried out the "the first International *C. elegans* Experiment in Space" (ICE-First). In the ICE-First experiment, we found that muscle-, metabolic-, and aging-related genes showed 10–20% lower expression levels in response to spaceflight. These studies were carried out in a chemically defined medium, which allowed study of the effects of surface tension in flight but which significantly alters *C. elegans* life history in a manor akin to dietary restriction.

4. In this study, we wished to confirm that gene and protein expression changes observed in ICE-FIRST were not unique to the operational issues associated with that spaceflight, were not owing to the use of a non-standard laboratory diet, and were owing to exposure to microgravity. To achieve these goals we flew worms on a different launch system, cultured them in a different segment of the ISS, froze them on orbit, used the standard nutritionally rich bacterial diet, and cultured them both in microgravity and on a 1-G centrifuge onboard the ISS. In our previous study ICE-First, worms exposed to microgravity showed ~20% lower expression of thick filament components such as myosin heavy chain and paramyosin upon return to Earth. In the current study CERISE, changes in the expression of these same genes were found in the worms grown in microgravity versus in those grown at 1 G (changes were 53–71%). These results confirm that the past reported gene and protein expression changes for C. elegans during spaceflight are not unique to specific operational constrains or diet, and are owing to microgravity. In addition to alterations in cytoskeletal genes we have observed reproducible changes in metabolic genes including sirtuin, which is also known to influence ageing. Consistent with the gene and protein expression changes we also found lower fat accumulation and shorter body length in the microgravity-exposed worms. Last, alterations in the movement of the microgravity worms were observed. These results demonstrate a reproducible set of C. elegans gene and protein expression changes in response to microgravity and provide the basis for future mechanistic studies of how microgravity impacts muscle alteration and metabolism in C. elegans and possibly astronauts.

Results

Proteomic and transcriptomic analysis of space-flown C. elegans

5. To identify proteins that were differentially expressed in the nematodes during spaceflight, we quantitatively analyzed the expression levels of 475 proteins by matrix-assisted laser desorption/ ionization time-of-flight tandem mass spectrometry. This analysis revealed significantly increased expression of 16 proteins and significantly decreased expression of 43 proteins in microgravity ($P \le 0.05$). Of the 16 proteins with increased expression, the expression of ASP-1 (aspartic protease) was increased 1.89-fold ($\log_2[\mu G/1\ G] = 0.92$) with the remaining proteins only slightly increased; these include proteins involved in protein synthesis such as ribosomal proteins and translation elongation factors (Figure 1). Gene expression analysis confirmed the downregulation of muscle-related proteins such as the myosin heavy chains, troponins, and intermediate filaments in the microgravity-cultured worms (Figure 1). Importantly, the pattern of downregulation of expression of muscle genes such as myosin heavy-chain genes myo-3 ($\log_2[\mu G/1\ G] = -0.89$) and unc-54 ($\log_2[\mu G/1\ G] = -0.49$) as well as the paramyosin gene unc-15 ($\log_2[\mu G/1\ G] = -0.62$) were reproducibly observed in both the current experiment and the previous flight experiment.

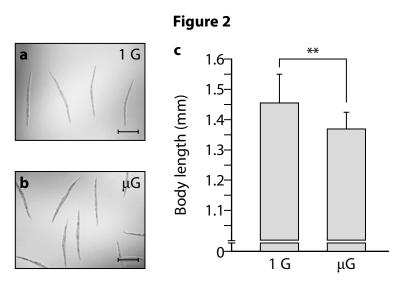


Quantitative analysis of protein (iTRAQ) and gene expression (microarray) levels in space-flown worms. The levels of certain muscular, cytoskeletal, and mitochondrial proteins and an aspartic protease (ASP-1) were significantly altered in worms cultured under microgravity conditions. $*P \le 0.05$, $**P \le 0.01$, Student's *t*-test for analyses.

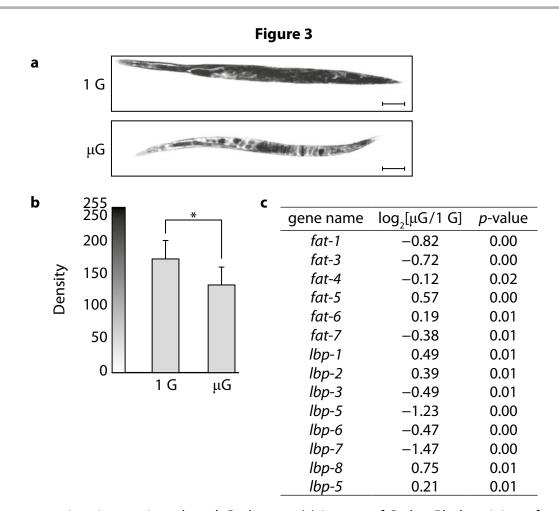
- 6. Other cytoskeletal components also displayed decreased expression during culture in microgravity, for example ACT-5 (actin), ATN-1 (α -actinin), DEB-1 (vinculin), IFB-2 (intermediate filament), and ANC-1 (nuclear and mitochondrial anchorage protein. In addition, significantly reduced levels of metabolic proteins were observed during culture in microgravity, for example, components involved in glycolysis (GPD-3), gluconeogenesis (PCK-1: phosphoenolpyruvate carboxykinase), and the glyoxylate cycle, a variation of the tricarboxylic acid (TCA) cycle (GEI-7). Moreover, the levels of components of the electron transport chain (SDHA-1) and the TCA cycle (ACO-2 and CTS-1) also significantly decreased during spaceflight. DNA microarray analysis confirmed these decreased protein expression levels in response to microgravity and suggested other energy metabolism gene expression level changes in microgravity. For example, genes encoding NADH dehydrogenase (complex I) and succinate dehydrogenase (complex II) displayed lower gene expression levels in the worms cultured in microgravity versus those cultured on the 1-G centrifuge (complex I: $\log_2[\mu G/1 G] = -0.18$ to -1.03, complex II: $\log_2[\mu G/1 G] = -0.56$ to -0.76). Similarly, ATP synthase expression was down ($\log_2[\mu G/1 G] = -0.38$ to -0.76).
- 7. Whereas DNA microarray analysis suggests that major muscle components, cytoskeletal elements, metabolic genes, and mitochondrial electron transport genes largely are downregulated in microgravity, some genes in these broad classes appear to be upregulated. Notably, a sirtuin gene, sir-2.1 encoding SIRT-1 protein, was upregulated. Sirtuin proteins deacetylate histones and several transcriptional factors, resulting in the activation or repression of target genes, and the sirtuin family may act as a global regulator of tissue health in response to diet and other stimuli. It was reported that sir-2.1 is involved in longevity and anti-aging of *C. elegans*, and that abu-6, abu-7, and pqn-5 are downstream targets that are negatively regulated by sir-2.1. Our microarray data indicate not only that the expression level of sir-2.1 significantly increases in microgravity but also that the downstream target gene expression levels significantly decrease under microgravity condition; notably, significant changes in the same directions of expression alteration were also noted on our previous flight. Real-time quantitative PCR (qPCR) analysis confirmed the increased expression of sir-2.1 and the decreased expression of downstream genes, which are negatively regulated by sir-2.1, including abu-6, abu-7, and pqn-5.

Body length and fat accumulation of nematodes cultured in microgravity

8. As proteomic and microarray analyses demonstrated decreased muscle and metabolic gene expression in microgravity, body lengths of a small subset of worms not used for omic analyses were microscopically measured. The body length of worms cultured in microgravity were slightly but significantly decreased by ~5.5% versus worms cultured on the centrifuge (μ G: 1.37 \pm 0.053 mm, 1 G: 1.45 \pm 0.094 mm, n = 15 worms per group, $P \leq$ 0.05; Figure 2). The data from the omics analyses suggest that the space-flown worms had lower energy metabolism capacity. Several molecules involved in fat metabolism are downstream targets of sirtuin signaling. Our DNA microarray analyses indicated that microgravity induced the decreased expression of *fat* genes encoding fatty acid desaturases and *lbp* genes that are involved in lipid binding activity (Figure 3c). The *sir-2.1* downstream target genes *fat-7* and *lbp-6* were among the downregulated transcripts ($\log_2[\mu G/1 G] = -0.38$ (P = 0.01) and -0.47 (P = 0.00), respectively). Therefore, we assessed lipid stores in a small subset of worms not used for omic analysis. Sudan Black staining indicated that the accumulation of fat in microgravity-cultured nematodes was significantly reduced compared with 1-G cultured worms (Figure 3a,b).



Alteration of body length of space-flown *C. elegans*. (a) Microscopic image of worms grown on the 1 G centrifuge for 4 days. (b) Microscopic image of worms grown in microgravity for 4 days. The worms in both conditions had normal levels of eggs in their bodies. (c) The mean of body length of the worms grown at 1 G was 1.45 ± 0.09 mm, and for microgravity was 1.37 ± 0.05 mm, respectively (n = 15, means \pm s.d.). ** $P \le 0.01$, Welch's t-test. Scale bars indicate 0.5 mm.



Altered fat storage in microgravity-cultured *C. elegans*. (a) Images of Sudan Black staining of accumulated fat in *C. elegans*. Worms grown onboard the 1 G centrifuge (upper image) and in microgravity (lower image) are displayed. Scale bars indicate 100 μ m. There was less fat accumulation in microgravity-cultured worms compared with 1 G controls. (b) Density measurements of Sudan Black stained worms (as described in Methods). The mean densities were 135.36 \pm 28.12 in microgravity-cultured worms and 176.55 \pm 27.61 in 1-G cultured worms (means \pm s.d.). * $P \leq 0.05$, Student's t-test. (c) Alteration of fat-related gene expression determined by microarray analysis. P-values as indicated in the panel, Student's t-test.

Effect of microgravity on swimming behavior of *C. elegans*

9. To examine the swimming behavior changes of *C. elegans* during spaceflight, we analyzed the swimming motion of worms grown under microgravity or 1 G on the ISS for 4 days. As shown in Table 1, wavelength showed no difference between microgravity and 1-G cultured worms. However, frequency of swimming was significantly different, and this likely caused a significant difference in wave velocity. Amplitude was measured at the point of 0.1 L, and no significant difference was observed. These results suggest that microgravity induced lower beating frequency and slower wave velocity without changing the shape feature of movement, i.e., the movement of the worm became slower under microgravity.

Table 1: Characteristics of moving behaviors of space-flown nematodes

Culture condition	μ G (n = 6)	1 G (n = 3)	<i>P</i> -value
Wavelength (L)	2.29 ± 0.71	2.07 ± 0.30	>0.1
Frequency (Hz)	1.53 ± 0.64	2.61 ± 0.12	<0.01
Wave velocity (L/s)	3.19 ± 0.76	5.39 ± 0.64	<0.01
Amplitude (rad/L)	4.09 ± 0.76	4.75 ± 0.40	>0.1

Discussion

10. It is well known that microgravity exerts considerable effects on physiological processes. Muscle atrophy is one of the main concerns for astronauts during spaceflight. To counter atrophy, astronauts are forced to perform several exercises such as using an ergometer. In 2004, we had the opportunity to conduct an experiment using the nematode *C. elegans* on the ISS. Nematodes flown in microgravity for ten days exhibited reduced gene expression of muscle-related molecules. Both gene and protein expression levels of myosin heavy chain and paramyosin, main components of thick filaments in invertebrates, significantly decreased in space-flown worms. In the present study, we also observed lower expression levels of both the major components for myofilament assembly such as myosin heavy chain and paramyosin. This repeated observation suggests that these changes are caused by spaceflight and not operational, technical, or dietary differences between these two spaceflight experiments.

References and Acknowledgements

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Microgravity elicits reproducible alterations in cytoskeletal and metabolic gene and protein expression in space-flown *Caenorhabditis elegans*

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