UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualifications:-

B.Sc. *B.Sc. (Intercal)*

Frontiers in Inflammation and Immunity

COURSE CODE	:	**IMMN3009**
UNIT VALUE	:	**0.50**
DATE	:	**12-MAY-06**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

TURN OVER

IMMN3009 FRONTIERS IN INFLAMMATION AND IMMUNITY

Candidates must answer **Sections A, B and C**. Please answer each section in a separate book.

The fraction of the total marks allocated to each section is as follows:

Section A: 60/180
(**essay**, 1 out of 3)

Section B: 60/180
(**short answers**, 3 out of 6)

Section C: 60/180
(**data interpretation**, 1 out of 1)

TURN OVER

SECTION A

Choose **ONE** question from the list below:

1. Describe the mechanisms that are involved in the control of new blood vessel formation (angiogenesis) in health and disease.

2. What is 'antigen' for T cells and how is it presented?

3. Discuss the key features of the granulomatous response, and explain how new molecular approaches have increased our understanding of the underlying mechanisms.

SECTION B

Write short notes on **THREE** of the following:

1. Free radicals and telomeric length.

2. Discuss the impact of promiscuous gene expression in the thymus.

3. Describe the classes of chemokines based on their primary structure.

4. Disease specific complement deficiencies.

5. The molecular basis of MHC polymorphisms.

6. What are the NALP3 associated hereditary fever syndromes? What is known about their inheritance, and what have these syndromes revealed about the regulation of IL-1 production in man?

CONTINUED

SECTION C

Answer **ALL** the questions, based on data from the paper.

This paper investigates which molecules are required for the development of functional natural killer (NK) cells in mice.
Glossary:
NK1.1, a molecule on NK cells which activates the cell when cross-linked.
Ly49A, a C-type lectin on NK cells that recognises a specific MHC molecule.
Ly49C, a C-type lectin on NK cells that recognises many MHC molecules.

Figure 1

1. Which surface molecule(s) do these experiments demonstrate are required for the development of functional:
   a) Ly49C +ve
   b) Ly49A +ve
   NK cells in mice? (10 marks)
2. Why are cells from Rag2 deficient mice used in Panel C? (3 marks)
3. Why are YAC-1 and CHO cells killed by NK cells? (2 marks)

Briefly describe the various types of inhibitory receptors expressed on NK cells of mice. (20 marks)

Figure 2

1. Which molecule do these experiments demonstrate is required for the development of functional NK cells? (5 marks)
2. Which region of this molecule is necessary? (5 marks)
3. Which stem cells give rise to NK cells? (5 marks)

This experiment uses a retroviral vector for gene expression in haematopoietic cells. Describe another a) experimental and b) clinical application of retroviral vectors. (20 marks)

Figure 3

1. What is the role of the SHP1 phosphatase in NK cell development? (5 marks)
2. Why are the mixed chimaeras used in panel b? (5 marks)

Describe the role of SHP1 in mature NK cell function. Discuss the role of other phosphatases in regulation of the immune system. (20 marks)

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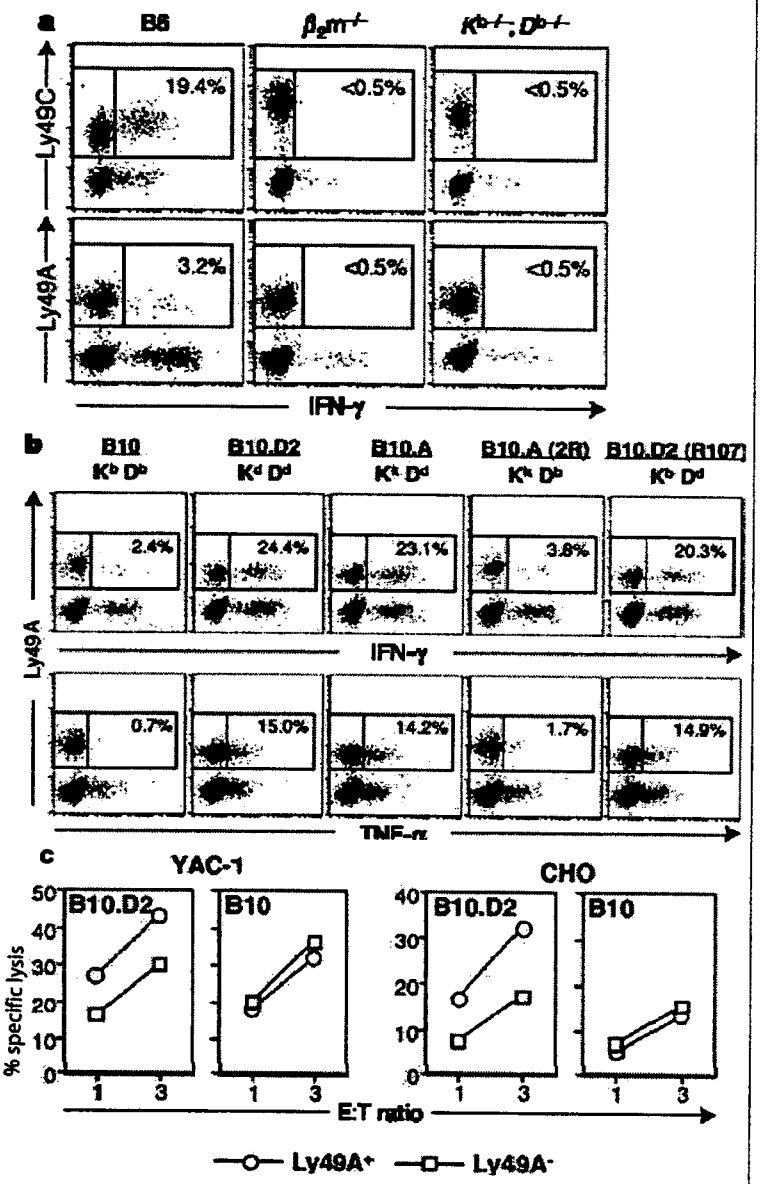

Figure 1. a) and b) Splenocytes from the indicated mouse strains were incubated with immobilized anti-NK1.1 antibody and analyzed for intracellular IFN-γ or TNF-α . The numbers represent the percentages of cytokine-producing cells among the Ly49A or Ly49C +ve populations. c) Ly49A+ve and Ly49A-ve cells were sorted from the spleens of Rag2 deficient B10 or B10.D2 mice and used in killing assays against the indicated target cells.

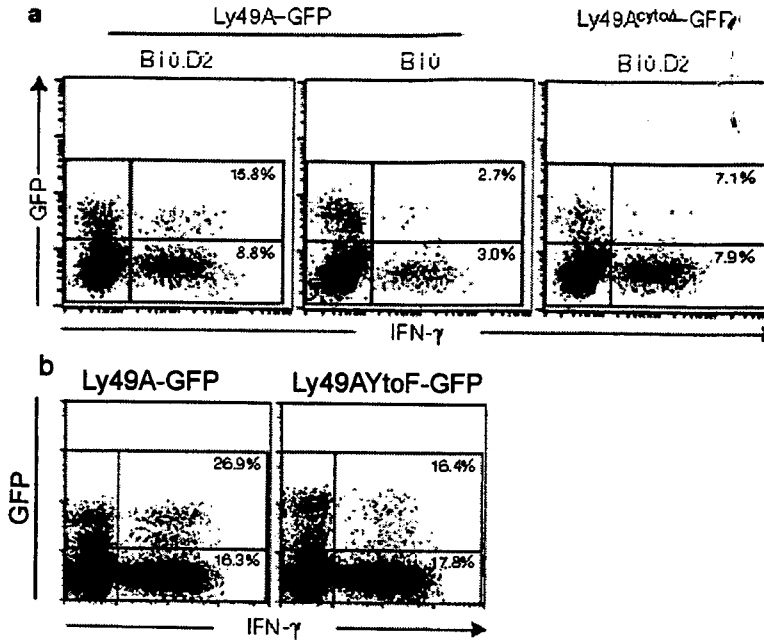

Figure 2. Mice were reconstituted with syngeneic bone marrow cells after transduction with a retroviral vector expressing Ly49A plus GFP, or Ly49A with the cytoplasmic tail deleted plus GFP, or Ly49 with Tyr in the ITIM mutated to Phe plus GFP as indicated. The numbers represent the percentages of cytokine-producing cells among the GFP +ve or -ve cells.

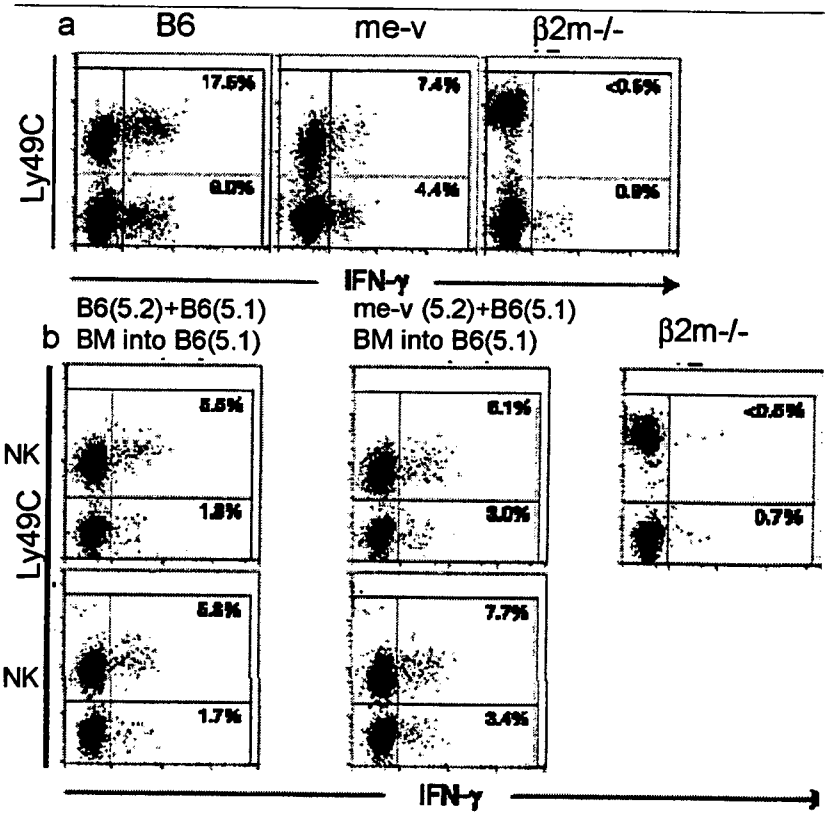

Figure 3. Splenocytes from the indicated mouse strains were incubated with immobilized anti-NK1.1 antibody and analyzed for intracellular IFN-γ. me-v is the motheaten-viable mouse mutant that lacks expression of the SHP1 phosphatase. The Ly5 molecule has two alleles Ly5.1 and Ly5.2 that can be distinguished using monoclonal antibodies. Mixed BM chimaeric mice were produced by injection of Ly5.2$^+$ B6 plus Ly5.1$^+$ B6 or Ly5.2$^+$ *me-v* plus Ly5.1$^+$ B6 BM into irradiated LY5.1$^+$ B6 mice and analysed after 9 weeks.

END OF PAPER