第一大題

I. Systematic screening of 250,000 bacterial extracts from 83,000 strains in three growth conditions, with the aim to identify chemicals against bacterial growth, led to the identification of a potent and selective small molecule from a strain of *Streptomyces platensis* recovered from a soil sample collected in South Africa. This molecule was named platensimycin ($C_{24}H_{27}NO_7$, relative molecular mass 441.47). The chemical structure of platensimycin is shown in Fig.1a. The *in vitro* toxicity of platensimycin against several strains of bacteria (including methicillin-susceptible, methicillin-resistant *Staphylococcus aureus*), HeLa cells and *Candida albicans* were shown in Table 1 with IC_{50} (concentration that inhibited 50% cell growth) indicated. Linezolid is a chemical which has been in clinical use since 2000. Carefully examine the figure and the table, answer the followings:

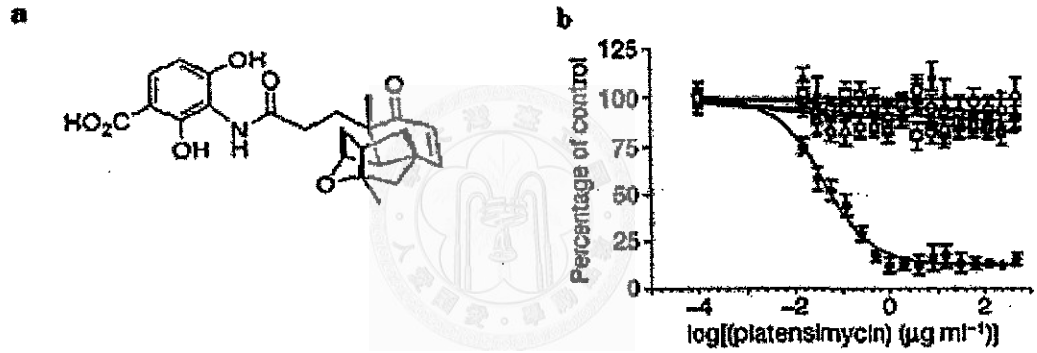

Fig. 1

a, Structure of platensimycin.

b. The assay was performed with a serial dilution of platensimycin, starting at 500 μg ml^{-1}. Effect of platensimycin on the synthesis of DNA (open circles), cell wall (filled triangles), protein (open squares), RNA (open triangles), and phospholipid (filled circles) were shown.

1) What is the primary mode of action of methicillin ? (2%)
2) List two possible mechanisms mediating methicillin-resistance in *S. aureus*. (2%)
3) Whole-cell labelling assay was performed to investigate the mechanism of action of platensimycin and shown in Fig. 1b. What might be the target of platensimycin ? (3%)
4) Please define "antibiotics".(2%)　Is platensimycin an antibiotic ? (1%)

見背面

Table 1 | Microbiological profiles and toxicity of platensimycin and linezolid

Organism and genotype	Platensimycin	Linezolid
Antibacterial activity	IC_{50} (μg/ml)	IC_{50} (μg/ml)
S. aureus (MSSA)	0.5	4
S. aureus + serum	2	4
S. aureus (MRSA)	0.5	2
S. aureus (MRSA, macrolide^R)	0.5	2
S. aureus (MRSA, linezolid^R)	1	32
S. aureus (VISA, vancomycin^I)	0.5	2
Enterococcus faecalis (macrolide^R)	1	1
Enterococcus faecium (VRE)	0.1	2
S. pneumoniae†	1	1
E. coli (wild-type)	>64	>64
E. coli (*tolC*)	16	32
Toxicity (μg ml^{-1})		
HeLa MTT	>1,000	>100
Candida albicans	>64	>64

*A concentration of 1 μg ml^{-1} equals 2.27 μM for platensimycin and 2.96 μM for linezolid.
†Cells were inoculated at 10^5 colony-forming units followed by incubation overnight at 37 °C with a serial dilution of compounds in Todd-Hewitt broth.
Linezolid is a synthetically derived agent that has been in clinical use since 2000. MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide; VISA, vancomycin-intermediate *S. aureus*; VRE, vancomycin-resistant *Enterococcus*.

II. Fill in the blank on the left column with the letter from the right column so that disease(s) and bacteria pathogen(s) are matched (12%)

Bacterial pathogen	Disease(s)
1. *Borrelia burgdorferi*	a. Diarrhea, hemolytic uremic syndrome (HUS)
2. *Streptococcus mutans*	b. Whooping cough
3. *E. coli* O157:H7	c. Meningitis, pneumonia, sinusitis
4. *Haemophilus influenzae*	d. Gastric and duodenal ulcers
5. *Staphylococcus aureus*	e. Food poisoning, wound infections, toxic shock syndrome
6. *Corynebacterium diphtheriae*	f. Food poisoning, gas gangrene, uterine infections
7. *Mycobacterium tuberculosis*	g. Diphtheria
8. *Helicobacter pylori*	h. Listeriosis
9. *Bordetella pertussis*	i. TB (tuberculosis)
10. *Treponema pallidum*	j. Syphilis
11. *Clostridium perfringens*	k. Lyme disease
12. *Listeria monocytogenes*	l. Dental caries

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III.

1) Define "normal flora". (2%)
2) What are the beneficial effects of Normal flora ? (2%)
3) While most of the activities of the normal flora benefit their host, some are **pathogenic** (capable of producing disease). How can we live in peace with these potentially noxious bacteria in our guts? Express your opinions. (4%)

第二大題

一、　下列敘述是否正確，正確者請答(○)，若有錯誤請打(x)，並修正錯誤之處，才予計分。(每題三分，共 15 分)

1. 病毒的基因體可以是 DNA 或 RNA，也可能是單股或雙股結構。
2. 核苷酸類似物和干擾素，是目前臨床上常用的兩種抗病毒藥物，兩者之作用機制，均在直接影響病毒 RNA polymerase 複製病毒基因體的步驟。
3. Herpes simplex virus 感染口腔部位時，會造成唇疱疹(cold sores)，臨床上常見此病毒會再次感染，不過復發時其症狀通常較初次感染輕微。
4. Human papillomaviruses 和 picornaviruses 均為 RNA 病毒，前者是造成子宮頸癌的主要致病原，後者則可能引起小兒麻痺和手口足病(hand-foot-and-mouth disease)等。
5. 水痘、德國麻疹、玫瑰疹、麻疹和傳染性紅斑(又稱 fifth disease)為兒童的五種發熱出疹性疾病，其中玫瑰疹常出現在臉上，其特殊的外觀類似 "被打了巴掌的雙頰"。

二、舉出三種肝炎病毒，並說明他們的基因體特性和主要的傳染途徑。(5 %)

三、兩個幼稚園的小朋友，因嚴重急性腹瀉，來到醫院求診。你如何推測其可能的感染原？試就你所認識的病毒，舉出兩種可能造成小朋友嚴重急性腹瀉的 RNA 病毒，並藉由此病毒的特性，說明如何由檢體進行檢測分析確認。(5 %)

四、請列出 MMR 疫苗可用於預防什麼病毒感染，並舉出其中的一種病毒，說明其基因體特性和感染此病毒時的主要臨床症狀。(5 %)

見背面

第三大題

1. 解釋名詞(各 3 分)
   A. Innate immunity
   B. anergy
   C. positive selection
   D. clonal selection
   E. Affinity maturation
   F. alloresponse

2. You cross two inbred strain mice A and B to have F1, then you further cross these F1 to get F2. If you transplant the skin graft from parent mice A to one of the F2 mice, what will be the chance the skin graft is rejected? (單選, 3 分)
   A. 100%　B. 75%　C. 50%　D. 25%　E. 0%

3. Which of the following vaccine is most effective in preventing infection? (單選, 3 分)
   A. live attenuated virus　B. heat killed virus
   C. genetically engineered recombinant viral virulent proteins
   D. DNA vaccine encoding viral proteins　E. non of the above, it depends case by case

4. 配合題: pick up the right answer from the below list (單選, 共 16 分)

_____ (1) viral antigens
_____ (2) tumor antigens
_____ (3) PGYAVEDGGMLL peptide
_____ (4) bacterial antigens
_____ (5) hypermutation
_____ (6) RAG-1
_____ (7) anaphylaxis
_____ (8) tuberculin test reaction

(A). MHC class I antigen presentation
(B). MHC class II antigen presentation
(C). non classical MHC antigen
(D). antigen binding sites in T cell receptor (TCR)
(E). NK cell receptor
(F). Initiate the cutting of recombination sequence-specific DNA cleavage during Ig gene rearrangement
(G). affinity maturation
(H). generation of memory cells
(I). Class switching
(J) Type I hypersensitivity
(K) Type II hypersensitivity
(L) Type III hypersensitivity
(M) Type IV hypersensitivity

試題隨卷繳回