

## 平成19年度大学院医学研究科（1回目）

### 医学・生物学一般試験（問題用紙1枚、解答用紙2枚）

以下の4問題から2問題を選択して解答しなさい。1問題につき1枚の解答用紙を使用すること。紙面不足の場合は裏面使用も可。

問1 医療安全管理の観点から、フェールセーフの概念の意味する所について実例を挙げて述べよ。

問2 次のことばを全て正しく使って RNA 干渉(RNAi)について 400 字程度で説明せよ。また、応用例についても記載せよ。必要に応じて図を使用しても良い。

(使用することば)

短鎖干渉 RNA (siRNA)、ダイサー、RNA 誘導サイレンシング複合体(RISC)、相補的、標的 RNA、mRNA、遺伝子発現、翻訳

問3 細胞に電極を刺入するときなどに細胞の表面に抵抗が在る事から細胞表面には何らかの境界構造が在る事が予想されていたが、その構造が判ったのは電子顕微鏡による細胞観察が行われてからである。その構造は“単位膜(Unit membrane)”または“生体膜”と呼ばれている。“単位膜(Unit membrane)”は、細胞内の膜系の殆どを構成している、極めて重要な構造である。特に膜系を構成する“単位膜”は“生体膜(Bio-membrane)”と呼ばれている。この“単位膜(Unit membrane)”または“生体膜”について説明せよ。

問4 疫学研究に用いられるコホート研究 (cohort study) および症例対照研究 (case-control study) について、それぞれの方法の利点と欠点を対比させる形で説明しなさい。

平成19年度大学院医学研究科（1回目）

受験番号

外国語試験問題・解答用紙（日本人）

下記の英文を読み設問に答えなさい。

Other countries in Africa began to wonder if they too might put emphasis on promoting fidelity and delayed age of sex, not necessarily instead of condoms, treating STDs and being testing—but in addition to these (Q1) “risk reduction” interventions. Such interest led to instant backlash. There were dark hints about right wing plots to force everyone into total abstinence. Rarely was reduction in numbers of sex partners actually discussed; the easier target was always “abstinence only.” But lest anyone think partner reduction was even feasible, many Western AIDS experts clamed that, “African men cannot be faithful,” “Africans are polygamous by nature,” “African women might abstain only to be infected by their husbands,” “not everyone can be faithful so it would be stigmatizing to expect anyone to be faithful,” etc, etc. Fidelity and abstinence programs were and are routinely dismissed as unrealistic, while condom programs are said to deal with people “as they actually are” rather than how we might wish them to be. Yet the best current biological and survey data simply do not support the popular image of the promiscuous African. According to UNAIDS, Sub-Saharan Africa now has an average HIV prevalence rate of 7.2%, down from 7.3% in 2004 and 7.5% a year earlier. This means that about 93% of Africans ages 15-49 are not HIV infected. If we consider all ages and include both the sexual inactive and North Africans as well, we can say that (Q2) about 97% of all Africans are HIV-free. If this is so contrary to everything we have heard, we can also calculate simple numerator over denominator: there are about 25.5 million infections in a total African population of about 840 million, meaning 3% infected and 97% uninfected. The broad trend in Africa is in fact toward higher levels of monogamy, fidelity, and abstinence, and the trend in HIV prevalence is incrementally downward. We now see HIV prevalence decline in Kenya, Zimbabwe, Senegal and probably other African countries as well. These welcome trends have come about in spite of the paucity of programs aimed at promoting fidelity and abstinence. The United States is the first major donor to include such programs in global AIDS prevention. This initiative should be applauded and supported, not condemned as a ploy to impose “abstinence-only” on Africa or the world. To illustrate the importance of AB factors (Abstinence and Being faithful, from Uganda’s ABC prevention model, where C means Condoms), let us consider Rwanda, the first example in the Washington Post article cited above(\*not included in the quoted sentences). Most experts assume that instability, civil war, genocide, breakdown of law and order—in short, social instability—would both predict a high HIV prevalence rate and would limit the ability of Africans to practice AB behaviors. Yet DHS and surveillance data from Rwanda amount to powerful evidence that these factors may have less impact than assumed. As we saw, a careful population-based survey recently found that Rwanda has a 3% national HIV prevalence, significantly lower than Uganda at present, and much lower than earlier UNAIDS estimates.

(Quoted from “A Better Understanding of African AIDS and What to Do About it”: Edward C. Green, [http://www.aids.org/news/africa\\_aids\\_ted\\_06\\_04\\_13.html](http://www.aids.org/news/africa_aids_ted_06_04_13.html))

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外国語試験問題・解答用紙（日本人）

受験番号

Q1. 文中で述べられている AIDS risk reduction の方法をすべて書きなさい。

Q2. 著者が about 97% of all Africans are HIV-free と推測した理由を説明しなさい。

Q3. 問題文の内容を日本語 400 字以内で要約しなさい。

以下の文章を読んで設問に答えなさい。

Muscle cells contain two types of filament that are aligned along the long axis of the cell. Contraction occurs when the protein myosin in the ‘thick’ filaments reacts with another protein, actin, in the ‘thin’ filaments, causing the filaments to slide across each other, pulling the ends of the cell closer together. The process is fuelled by the breakdown of ATP. The biochemical basis of contraction was largely determined by Albert Szent-Gyorgyi in the 1940s, and the biophysical and structural basis was uncovered by Jean Hanson and Hugh Huxley, and by Andrew Huxley and R. Niedergerke, during the 1950s. But how the process was triggered by nerves remained a mystery. Ebashi discovered that in the absence of calcium ions, no contractile reaction occurs, even when ATP is added to the myosin-actin system, but that with even a minute amount of calcium (of the order of 1 micromolar), ATP induces a vigorous contractile reaction. This calcium-dependence had been previously overlooked by biochemists because of low level contamination from laboratory glassware and impurities in the chemical reagents. Ebashi took tremendous pains to avoid contamination by calcium ions in all the solutions and protein preparations he used, making his results unequivocal. His work was consistent with contemporary results from Annemarie Weber, who showed independently that the breakdown of ATP during the contractile reaction requires minute amounts of calcium.

The idea that calcium might be involved in muscle contraction came to Ebashi during his studies on the ‘relaxing factor’ reported by B. B. Marsh in 1951. This was a fraction of the homogenate that is made when muscle cells are ground up, and it could induce relaxation of the myosin-actin system. Ebashi proved that relaxing factor is nothing but fragmented pieces of a muscle-specific organelle called the sarcoplasmic reticulum. Enquiring into the factor’s mechanism of action, Ebashi got a hint from Emil Bozler’s result in 1954 that EDTA a ‘chelating’ agent that sequesters calcium causes relaxation. Ebashi compared the calcium-binding activity of various chelating agents with their relaxing activity and found that they correlated exactly. He further showed that fragmented sarcoplasmic reticulum can accumulate calcium ions rapidly in the presence of ATP, and so can remove enough calcium from the surrounding medium to cause relaxation.

The relaxation process is the reverse of contraction, so Ebashi proposed what is our current understanding of excitation-contraction coupling: excitation at the surface membrane somehow sends a signal to the sarcoplasmic reticulum; this releases the calcium ions that accumulate there during the relaxing and resting period, and the flood of calcium ions induces the contractile reaction. Examining the process more closely, Ebashi discovered that purified myosin and actin react with ATP even in the complete absence of calcium ions, and that the regulatory action of calcium is exerted only in the presence of a certain protein factor. This factor turned out to be a mixture of tropomyosin, a protein that previously had no known function, and a newly discovered protein that Ebashi named troponin.

Tropomyosin and troponin are present with actin in the thin filaments. In the absence of calcium ions, the two proteins cooperate to inhibit actin, preventing it from interacting with myosin in the thick filaments. Having found that calcium binds strongly to troponin, Ebashi proposed that the resulting conformational changes in troponin are transmitted through tropomyosin to actin to remove the inhibition, and the contractile reaction ensues—a mechanism that has subsequently been confirmed. In the early 1960s, the idea that a simple inorganic ion such as calcium controls contraction was not popular among most biochemists—the prevailing belief was that such an important biological phenomenon as contraction should be regulated by sophisticated organic molecules. So Ebashi had a hard time getting his ideas taken seriously, despite his clear evidence. Only after the discovery of troponin and his elucidation of the mechanism did everybody accept the regulatory role of calcium ions. The regulatory roles of calcium are not confined to muscle contraction. Since Ebashi’s discovery, numerous cellular processes, including the release of neurotransmitters and hormones, metabolic switching and gene expression, have been found to be controlled by calcium.

(Seturo Ebashi 追悼文 by Makoto Endo : Nature 442, 996, 2006 より抜粋)

平成19年度大学院医学研究科（1回目）

受験番号

外国語試験問題・解答用紙（日本人）

問題 1. (A) 研究の初期には、何故、筋収縮における calcium の重要性が注目されなかったか？ (B) Ebashi (江橋教授) はそれを明らかにするため何をしたか？

問題 2. 江橋教授は、EDTA (a chelating agent) の効果に関する Emil Bozler の報告を参考にし、(A) どのような研究を行い、(B) どのような発見につながったと考えられるか？

問題 3. Purified myosin と Purified actin は calcium がなくても相互作用をする。江橋教授は、(A) 何を発見し、(B) それはどういう仕組みで calcium による筋収縮を調節するのか？