Preface

科学技術の進歩は目覚ましく，日進月歩を超えた展開が日々生まれている。一方で基礎的な知見の確認と研究の忍耐強い積み重ねにより，科学技術の進展があることも忘れてはならない。生物学においては，学問の基本を理解するとともに，新しい知見の理解推進は必須のものである。今日では生物を見ることから生物から得られる多様な情報を利用するように変ってきており，日々大量の情報を検索し，研究に臨む必要がある。

先端的な研究課題については，日本国内の研究においても専門論文やインターネットでの情報は，世界共通言語ともいえる英語での記述が主流である。世界の権威ある科学雑誌や研究機関は当然ながら英語で情報を公開しており，英語での学問の理解は必須である。

本書は，前作の「英語で学ぶ生物学」を受け継ぎつつ，最近のトピックでありまた基礎的な事項としても理解が必要な題材を新たに提供している。それは幅広く題材を理解するための基礎的な情報を提供するとともに，また専門用語に慣れることを意図している。さらに生物学の知識の修得だけではなく，生物学に関わる倫理や社会の問題を同時に考察することも考慮している。

取り上げた各題材は，著者が世界の著名な研究雑誌や最近のニュースとなった話題から選抜したものであり，これらについて関連論文や書籍を精査し，その内容を独自にまとめたオリジナルなものである。世界中の多様な話題をすべて網羅するのではなく，日本と世界に共通した事項を選抜している。

各章はオムニバス形式でそれぞれ独立しているため，題材はどこからでも拾い読みすることができる。興味のある方々には，本文の後に掲載された参考書籍や文献を読むことで，さらに理解を深めていただければと期待している。なお基礎的な知見や専門用語については，「英語で学ぶ生物学」や，「英語で学ぶ医科学入門」「英語で学ぶ環境科学」（英語で学ぶ自然科学シリーズ）などを並

行して利用いただければ，さらに理解が進むことだろう。

科学技術は将来への多様な可能性を生み出すが，一方では，得られた知見の正しい適用や社会との透明性のある合意形成がなければ，人類が適正に享受することはできない。これは生物学においてもしかりであり，本書で取り上げた各章の Exercises では，単純に知見を英語で理解するだけではなく，知見の社会との関わりについて話題を提供し，学習グループや個別の読者がそれについて十分に考えることを期待している。

最後に，本書執筆にあたり長い期間ご支援くださった多くの関係者各位に感謝いたします。そして，本書が生物学およびその新しい知見利用の理解推進に資することができればと期待します。

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著　者

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Chapter 1

Discovery of Induced Pluripotent Stem Cells（iPS Cells）

Many of you have probably learned about planarians in a biology class. A planarian is an aquatic organism about 1 cm long that lives in cold water. Interestingly as in **Figure 1**, if you cut a planarian into four equal parts, the parts will regenerate to produce four planarians! In other organisms too, such as lizards or newts, regeneration occurs at areas where they have been cut. Even in humans, if you scratch your hand, the bleeding eventually stops and the scratched area slowly regenerates back to its original form. Among cells, the birth of these new cells results from the action of stem cells.

Stem cells are present in a variety of organisms. In a planarian, stem cells aggregate at wound openings and repair begins, after which a planarian completely identical to the original one is formed. Stem cells exist in humans as well, serving to replace damaged or aged cells or to newly replenish cells lost as a result of disease or injury. The only difference between stem cells in humans and those in planarians is that although human stem cells can regenerate, they are limited to producing only certain types of cells. Although a simple hand skin injury can be repaired, the restoration of large and complex parts such as whole arms and legs is impossible. These cells are known as adult stem cells.

In contrast to these adult stem cells, artificially created stem cells have also emerged on the scene. These cells, unlike adult stem cells, can turn into all manner of cell types. In 2006, a cohort of Japanese researchers generated the world's first iPS cells（induced pluripotent stem cells）from mice. These iPS cells, which were

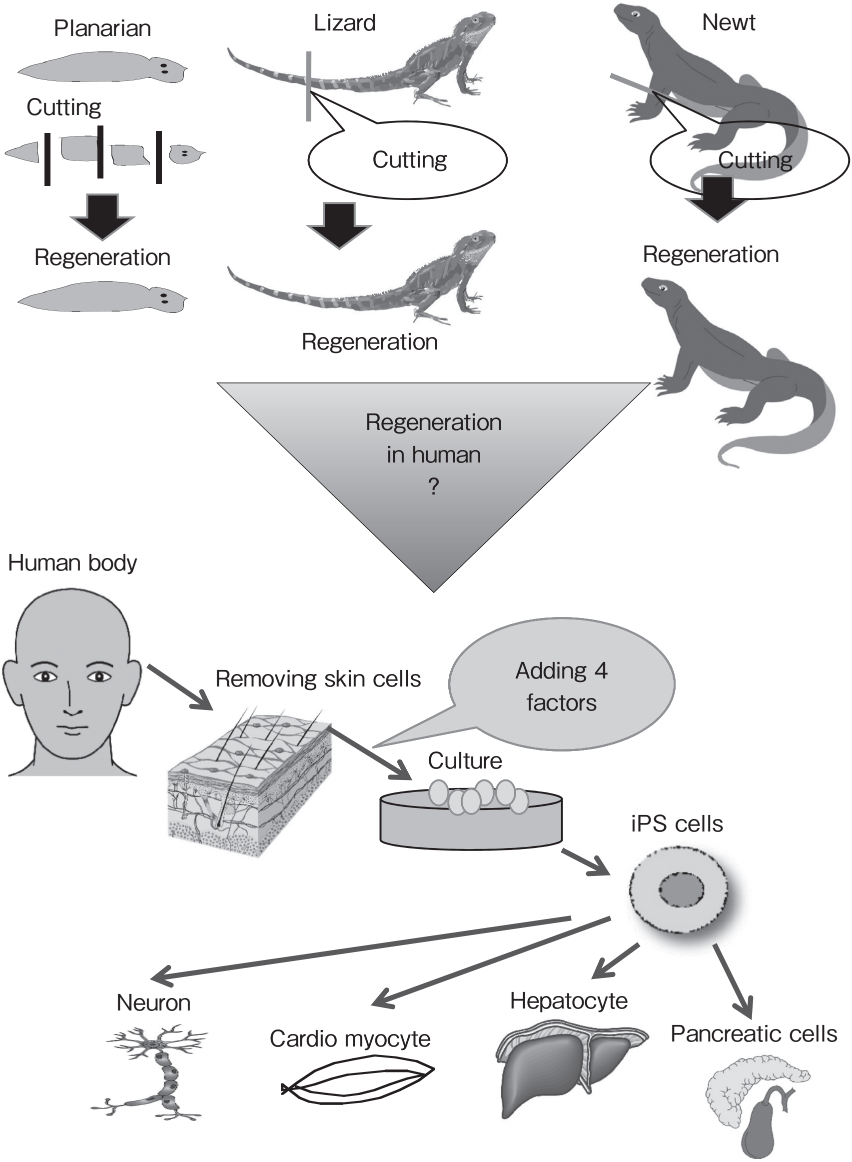

Figure 1 An idea for creating iPS cell production.

cultured from skin cells (fibroblasts) in mice, differentiated into cardiac muscle cells that beat in cell clusters. Two years later, the same technique was applied to cells obtained from human skin. News of this raced around the world in a flash.

These iPS stem cells differed greatly from the embryonic stem cells (ES cells) that had been used up until that time. Because fertilized eggs are not used to create iPS cells, the ethical barriers to their use are very low. In addition, immunological rejection is assumed not to occur because an individual's (the patient's own) skin cells are used.

A major catalyst for the discovery of iPS cells was the birth of Dolly the sheep in 1996. The nucleus taken from a mature udder cell of a sheep was inserted into an egg whose nuclei had been removed. When this egg was placed into the uterus of a different sheep, the newborn was completely identical to Dolly's genetic mother. This mysterious art produces what is known as a cloned embryo. This technique spectacularly overturned the conventional view until then that in mammals, cells that had differentiated would never rewind (become initialized). Four years later, in 2000, ES cells were produced.

A lizard's tail regenerates beautifully even if it is cut off. A newt's arm regenerates not only skin tissue but also bone when it is severed. Furthermore, as for planarians, they regenerate even after being cut into small pieces. In contrast, in mammals, starting from the time the egg is fertilized, cells become increasingly differentiated, finally turning into different organs, and it was thought that going in reverse was impossible; that is, that cells, once differentiated, could not possibly return to the initial egg cell, and that the process was a one-way street (irreversible). Nonetheless, the birth of Dolly and the production of ES cells demonstrated that this process could be rewound. Thus, the path toward the birth of iPS cells had begun.

The method of producing iPS cells is surprisingly simple. It is said that anyone with experience in basic genetic manipulation techniques and culturing may be able to produce them. However, it is taking time for this method to become established. Particularly important aspects are the genes that need to be introduced into non-pluripotent cells to force them to become iPS cells. Studies on ES cells thus far provided numerous hints, and the to-be-introduced genes were ultimately narrowed down to four（the Yamanaka factors）: those that 1）build the body, 2）play a key role in expression, 3）play an important role during regeneration, and 4）control transcription. Each of these genes is introduced into the cell via a *retrovirus*. Genes for 3）can carry a risk of causing cancer, but these can now be avoided.

Although the method of using *retroviruses* to introduce genes has great advantages, some genes cause adverse effects on the body, particularly in gene therapy. Hence, methods to directly produce iPS cells without the insertion of genes are also being explored.

The most innovative aspect of iPS cells is that they can be used for transplants and regenerative medicine. Given that iPS cells are cultured from the patient’s own skin, there is unlikely to be immunological rejection. Currently, ideas such as preparing pools of cells according to the type of *human leukocyte antigen*（HLA）are being considered so that they can be used immediately when needed. These iPS cells could be applied to the treatment of various diseases. In mice, researchers have succeeded in producing blood stem cells from iPS cells and applying them to the treatment of *sickle-cell anemia*. There are also reports that transplanting neural stem cells derived from iPS cells into mice artificially given spinal injuries

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Notes：*retrovirus*「レトロウイルス」，*human leukocyte antigen*（HLA）「ヒト白血球抗原」 *sickle-cell anemia*「鎌型赤血球症」

reduced the symptoms by 20％. iPS cells, which are capable of becoming various tissues, are being considered for practical use in the treatment of diseases such as *Parkinson's disease*, *muscular dystrophy*, *myocardial infarction*, and diabetes, and positive outcomes of such work have been confirmed. Research is being advanced at core universities in Japan, beginning with experimental animals such as mice and working toward eventual application in humans.

Conversely, iPS cells can also help reveal the causes of various diseases. By producing stem cells from the cells of diseased patients, it will become possible to study how and why diseases occur when they do. Until now, tissues have been directly taken from diseased patients and cultured; but such cells hardly ever proliferate, and this is also a great burden for the patients. However, by using iPS cells derived from the cells of diseased patients, we are about to understand how pathogenesis occurs. For example, the increasingly rapid cell loss that occurs in *amyotrophic lateral sclerosis*（ALS）has been revealed visually as well.

iPS cells are also expected to bring about ground-breaking progress in drug research. In the past, candidate drugs were first screened in experimental animals such as mice, monkeys, or pigs and their effects were then tested by experimentally administering them to humans. However, a drug that was highly effective in animal experiments might show a reduced effect, a rejection response, or toxicity when administered to people. An enormous amount of time and effort is considered necessary in order to discover just one drug in the conventional way; however, if iPS cells are used, animal experiments will become unnecessary. By transforming the cells into

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Notes：*Parkinson's disease*「パーキンソンン病」
muscular dystrophy「筋ジストロフィー」，*myocardial infarction*「心筋梗塞」
amyotrophic lateral sclerosis（ALS）「筋萎縮性側索硬化症」

the desired tissue, the effects and toxicity of a drug can be confirmed.

Looking ahead, the day we can culture iPS cells in three dimensions and replace organs that have weakened or stopped functioning is not so far off. And though efforts to create human organs in the bodies of pigs have begun, there are many more problems that yet remain. To this end, there are many remaining challenges to be addressed concerning research on stem cells (including iPS cells), such as the consideration of ethical issues, establishment of systems and guidelines, financial support, and the understanding of the patients and general public.

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