Structure-editing: A New Branch?

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To the Editor: As we all known, structure determines and influences biological function and mechanisms. Biological structure-editing (SE) means by using those magical and novel technologies (including single, multiple, or hybrid) with biological hazard and challenge to edit or reform known and disclosed biological structures of different levels so that people can translate SE into basic research or clinical application. As a new branch of structure biology, the authors think that its field focuses mainly on several facets.

First, SE of *in vivo* system. It includes organ transplantation, defect reparation, replacement, and removal by surgical operation or interventional therapy. It is through the relevant biotechnology for the upgrading of human organs and returns to normal function. In recent years, transcatheter aortic-valve replacement (TAVR) has modified greatly the management of related structural heart disease.[1] A novel stepped management program for hypertension which included edited therapeutic program and healthy lifestyles,[2] and some catheter-based technologies are good strategies for structural and nonstructural heart diseases. They will form the basis of a macroscopic biological SE.

Second, SE of *in vitro* system. This includes a variety of tools from enzymes, cytokines, biomarkers, and virus vectors, etc., to a number of drugs or vaccines. As we all known, gene therapy needs a variety of virus vectors, such as adenovirus and adeno-associated virus. These viruses must be preprocessed, inactivated, and reduced in toxicity; some need SE in order to realize effective transfer gene and enhance its efficacy. As to the SE of cardiovascular drugs, this means better effect and safety, and fewer adverse reactions, such as the levorotatory of antihypertensive drug amlodipine, and some small molecular chemicals.

Third, SE of the molecule or cell level. The discovery of the structure of a special gene, receptor or protein, which associated with some major diseases, will lay a solid foundation for understanding the function and mechanism of specific genes or proteins related diseases. Specific biological SE will help for future drug design and combating these diseases. For example, it is possible that human AdipoR agonists for obesity-related diseases, such as obesity-obstructive sleep apnea-hypertension (OOH) syndrome. When obesity becomes an important and potential risk factor of cardiovascular, diabetes, cancer (CDC) strips,[3] some patients with obesity need clinical SE of *in vivo* system, such as bariatric surgery. Therefore, more complicated and original SE which based on the discovery of the crystal structure of related genes, receptors, or proteins is very important and promising. As reported in *Science,* an M-locus gene Nix knockout with CRISPR/Cas9 resulted in converting female mosquitoes into harmless males.[4] This confirmed that changing genes may lead to drastic changes in structure and function of subjects.

Just like unlimited scenery is in the risk place, there are some biohazards both in basic and clinical SE. For example, there is a higher incidence of stroke or transient ischemic attack in group patients with TAVR.[5] Therefore, the scientists and doctors should translate more SE technology [Table 1] with higher or lower biohazard and challenge but not ethical problems into their basic research or clinical development after disclosing those newer

Table 1: Classical methods of biological structure-editing

Methods	Molecule or cell level, *in vitro*, *in vivo*
1. A → A + X	Add or repair (e.g., ASD or VSD repair)
A → A – X	Decrease, remove, separate (e.g., induce apoptosis)
A → A + X – Y	First, add; then, reduce
A → A – X + Y	First, reduce; then, add (e.g., CABG, PCI + stent, TAVI, etc.)
2. A → a, a → A	Zoom in or out (e.g., PCR amplify)
3. A → B, B → A	Replace or translate (e.g., valve replace)
4. AB → BA, BA → AB	Conversion
5. ABCD → ACDB	Shift
6. ABCD → ANCD	Mutation
7. ABCD → ABC	Delete or shorten (e.g., telomerase and aging, gene knock-out, etc.)
8. A···· → ABCD	Rebuild RNAi or CRISPR/Cas9
9.··· → ABCD	Reprogramming, 3D biological printing

ASD: Atrial septal defect; VSD: Ventricular septal defect; CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention; TAVI: Transcatheter aortic valve implantation; PCR: Polymerase chain reaction; 3D: Three-dimensional.

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and more beautiful structures. In the future, biological SE will be not only a novel branch of biology and a new subject in studying biology and life science, but also a new choice in the era of precise medicine.

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Conflicts of interest

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