Bioengineering A Kidney - A Brief Review

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According to the National Kidney Foundation, an estimated 37 million US citizens currently suffer from kidney disease [(1)]. This number is expected to rise further due to the escalating prevalence of both high blood pressure and diabetes in the country [(2)], which are key contributing factors that amplify the risk of kidney disease. In advanced stage kidney disease, the only option often becomes kidney transplantation, with the organ coming from either a living or a deceased donor. However, the need for transplantable kidneys far exceeds the number of kidneys available. Until a kidney becomes available, patients with failing kidneys are offered dialysis. In this article I will review briefly the current approaches being undertaken to facilitate effective treatment for advanced stage kidney disease.

I Kidney function

The kidney plays an integral role in maintaining overall health and homeostasis. The kidney's filtering process begins as used blood from around the body is pumped to it for cleaning. The blood is meticulously filtered through the individual nephrons, effectively removing waste products and maintaining a proper balance. Following the filtration, the purified blood travels through a series of micro capillaries, transitioning from the renal vein to the renal artery, before ultimately being propelled through the heart and to the lungs for oxygenation. At the same time, waste products from the individual nephrons accumulate in the collecting duct and move into the ureter. The ureter serves as the conduit for transporting waste products, including urea, salt, sugar, and minerals, from the kidney to the bladder [(3)]. In this process, the kidney fulfills its important roles in cleansing the blood, regulating pH levels, and ensuring an appropriate salt balance. The complexity of these processes underscores the kidney's key role in maintaining bodily equilibrium and its vital role in overall well-being.

II Kidney development

The intricate development of the kidney begins with cell-to-cell interactions in the early embryo, within a specific area of the mesoderm layer. Cells in the mesoderm initiate the budding process, which then undergo further branching, resulting in an intricate network of nephrons, the fundamental filtration units of the kidney. Remarkably, each kidney contains approximately half a million nephrons. Interplay between cell populations in the developing kidney needs to occur at the right time and in the right order to correctly develop the organ [(4)]. If chemical signals are not communicated accurately the progress will stall and eventually fall apart. It has taken many years for biologists studying the kidney to understand this process enough to begin development efforts in the lab.

III Transplantation

Obviously, there are many more potential donors out there compared to the number of organs actually being offered [(5)]. One solution to this problem is to increase the number of donors through either education or legislation. For example, in many European countries, organ donation is the default and the person must actively opt out of the national donation system. It would help to make the entire transplantation process more affordable for the recipient patient, primarily through better insurance coverage. Finally, another possible solution is to utilize pig kidneys. Biologically, pigs are remarkably similar to humans, and the size of their kidneys are almost identical to ours. Tests with genetically modified donor kidneys from pigs have shown that it is possible to reduce the risk of rejection after transplantation [(6)]. This could often be a temporary measure to keep the patient healthy until a human or bioengineered kidney is made available.

IV Bioengineering a functional kidney in the lab

Addressing the need for more kidneys, bioengineering endeavors have created resourceful solutions. One approach involves the creation of transplantable kidneys through the use of stem cells. Stem cells, found in embryos, possess the remarkable potential to develop into a wide array of bodily tissues when properly guided. Because of the ethical concerns around harvesting stem cells from embryos, scientists were hard at work searching for a solution. This solution was found in Induced Pluripotent Stem Cells (iPSCs), which are taken from adults and reprogrammed back into an embryonic-like pluripotent state. These iPSC cells can be used almost interchangeably with stem cells and hold the advantage of deriving organs and tissues from the patients themselves [(7)]. This ingenious strategy involves the decellularization of the kidney, where all cellular content is removed, leaving behind a scaffold that can dictate the organization and differentiation of cells. By seeding the scaffold with kidney-specific stem cells or iPSC cells, these cells can integrate into the scaffold's architecture and respond to signaling cues. All of this combined with knowledge of growth factors in kidney development drives this process. This eventually results in the development of a functional kidney. Most importantly, the organ created in this manner is immunologically identical to the patient, negating the need for prolonged immunosuppression post-transplantation, which is a large concern for traditional organ transplantation.

V Bioengineering a miniature dialysis machine

Another promising development in the realm of kidney disease treatment is the bio-miniaturization of dialysis machines. Conventional dialysis involves rerouting the renal vein and renal artery into a large external machine, replicating the blood-filtering function of the kidneys [(8)]. However, this process takes place on a large scale, requiring extended periods of patient immobilization during each session, which occur several times a week. The interval between dialysis treatments places considerable strain on the body as toxins accumulate, leading to a decline in overall health and quality of life [(9)]. Tragically, a significant proportion of dialysis patients succumb to their disease within five years. To counteract these challenges, a groundbreaking approach aims to engineer a compact, transportable dialysis machine that more closely mimics the functions of a natural kidney [(10)]. This innovation not only offers enhanced efficacy compared to traditional dialysis but also holds the promise of restoring patients' quality of life by alleviating the burdens associated with frequent, time-consuming sessions. By providing a more efficient and convenient alternative, the bio-miniaturization of dialysis machines could potentially extend the lifespan and improve the overall well-being of patients. While a healthy human kidney can filter the entire body's blood content 20-25 times a day, a portable dialysis machine would probably be very useful even if it could not match that volume of blood.

VI Conclusions and future prospects

These incredible advancements make it possible that in the near future we will be creating functional kidneys in the lab or portable kidney machines. This holds out great hope for the large number of people suffering from end stage kidney disease which, as noted earlier, is bound to increase. Personally, I find these possibilities extremely exciting, and I hope that I may be able to be involved in this field in the near future.

References

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