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Towards predictive, preventive, and personalized paediatric surgery

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Abstract Future medicine will be revolutionized by genomic and stem cell research, becoming predictive, preventive, and personalized. Despite the smallness of the specialty, paediatric surgery is well placed to play a determining role in this exciting development. First, paediatric surgeons are innovators and leaders. Second, paediatric surgery thrives on the multidisciplinary approach. Third, congenital anomalies provide genetic models for studies of complex diseases. Fourth, morphogenesis underpins basic understanding in development, ageing, cancer, and immunology. The next generation paediatric surgeons must seize the opportunities in large-scale biology research to develop the best future treatment for their patients.
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1. The genomic and stem cell era

The British Association of Paediatric Surgeons was founded in 1953. Its objects are the advancement of study, practice, and research in paediatric surgery. In the same year, Watson and Crick discovered the structure of deoxyribonucleic acid (DNA) and modestly stated that "it has not escaped our notice that the specific paring we have postulated immediately suggests a possible copying mechanism for the genetic material" [1] In fact, the breakthrough has opened up our understanding of molecular biology and genetics in such a way that DNA now underlies every aspect of human health. Understanding gene and protein function will have a profound impact on diagnosis and prediction, prevention, and personalized treatment of diseases. Few will doubt that genomics will bring revolutionary changes in clinical and public health practice.

The double breakthroughs of animal cloning by Wilmut and Campbell in 1997 [2] and the first isolation of human embryonic stem cells by Thomson et al in 1998 [3] have generated much excitement both in the scientific community and the general public. Stem cell research offers much hope for cell-replacement therapies for many diseases, and such treatments can be potentially patient specific. The convergence of basic science and clinical medicine has never been closer.

2. Whither paediatric surgery

The question is, in this era of genomic and stem cell revolution fuelled by high-cost, fast-moving technologies and competing funding demands, where will paediatric surgeons be? Will we become mere bystanders and fringe players, or can we play a determining role in large-scale biology for the benefit of our patients?

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The odds are against paediatric surgery. It is a small specialty with small numbers of patients and researchers. To the general public and the policy makers, the diseases in paediatric surgery have low visibility and socioeconomic impact compared with cancer, ageing diseases, infection, etc. As a result, funding opportunities for basic and translational research for our specialty are limited.

I will, however, argue that we can overturn the odds. Just as paediatric surgery has now stolen the march in the development of minimal invasive surgery from adult surgery after a slow start, we have several advantages that will allow us to surf ahead on the crest of the waves of biomedical research. My arguments are as follows:

1. Surgeons in general and paediatric surgeons in particular are innovators and leaders.
2. Paediatric surgery thrives on multidisciplinary approach.
3. Congenital anomalies provide genetic models for studies of complex diseases.
4. Morphogenesis underpins basic understanding not only in development, but also in ageing, cancer, and immunology.

I contend that there are many examples to support the arguments; but without attempting to be exhaustive and comprehensive, I will illustrate some arguments with personal experiences.

3. Innovation and leadership

Surgeons are innovators and problem solvers. The history of surgery is annotated with breakthrough discoveries. The only medical advance to make it into *Life Magazine*'s top 10 most important advances of the previous millennium was the germ theory, founded on the works of a surgeon, Joseph Lister, on antisepsis. No less than 9 surgeons were awarded the Nobel Prize in Medicine and Physiology from 1901 to 2005 for works ranging from understanding the thyroid, to discoveries of cancer treatment, and to transplantation [4]. In the recent decades, one of the most important biomedical discoveries, angiogenesis, was made by a paediatric surgeon, Dr Judah Folkman [5].

Modern biological research is increasingly team based. Paediatric surgeons are good team players and effective team leaders. There are many examples of paediatric surgeons establishing themselves as leaders beyond their specialty. Dr CE Koop was Surgeon General of the United States, the nation's top administrative health post, in the 1980s. Surgical Associations and Colleges around the world have elected paediatric surgeons as their presidents, for example, J Grosfeld (American Surgical Association), K Anderson (American College of Surgeons), J Orr (Royal College of Surgeons, Edinburgh), A Kolbe (Royal Australasian College of Surgeons), etc. Universities and hospitals have appointed paediatric surgeons as heads, for example, F Cigarroa (Chancellor, University of Texas), WJ Chen (President, National Taiwan University), P Tam (Vice President, the University of Hong Kong). Leadership outside the specialty can bring benefit to paediatric surgery because policy makers will understand better children's needs and afford paediatric surgeons a more level playing field in the competition for research funding.

4. Multidisciplinary research

The "big science" nowadays is dominated by the multidisciplinary approach, an approach that many conventional scientists are still unaccustomed to. Paediatric surgeons have always cherished the multidisciplinary approach in clinical care and therefore are well positioned to extend this attitude to research. In the past decade, the most exciting research projects I have participated in have been multidisciplinary and have involved the establishment of expensive, cutting-edge technologies that single laboratories cannot afford.

5. Centre of human development and birth defect

I returned to the University of Hong Kong in 1996 and encountered all the difficulties that a researcher in a small clinical discipline would face, especially the lack of a critical mass of researchers to make an impact. However, as a paediatric surgeon, I was keen to reach out; and it soon became clear to me that developmental biologists similarly felt isolated. The clinicians have the problems, whereas the scientists have the tools. We founded the Centre of Human Development and Birth Defects in 1999 with the aim of linking clinicians and scientists to explore gene function in development and diseases. Model systems including mouse, rat, chick worm, fish, and frog were established. Transgenic and knockout mice were created. A congenital malformation registry with protocol-based sample collection was set up. Through regular meetings, research collaboration increased substantially. With increasing research productivity, the Centre expanded in size and funding, acquiring recognition as one of the University's strategic research themes and an Area of Excellence in Hong Kong. The Centre is now well placed to play a leading role in stem cell biology and regenerative medicine research.

6. Genome research centre

In 2001, the University of Hong Kong identified genomics as a major strategic research direction of the University and allocated a sum of HK$120 million (≈US$15 million) to establish the Genome Research Centre. The Centre provides the expertise and infrastructure in genomics, proteomics, and bioinformatics for scientists and clinicians to apply them for studies to understand and treat diseases. This signals the move

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