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Invited review article

Exploring the biology of the nail: An intriguing but less-investigated skin appendage

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ABSTRACT

The nail is a highly keratinized structure covering the tip of the digit, and considered to have several important functions in our daily life. In recent years, as biological aspects of the nail organ have been characterized, we realize that the nail unit and the hair follicle share various biological and immunological features. In particular, development and homeostasis of the nail unit also requires intimate epithelial–mesenchymal interactions that involve signaling pathways such as Wnt. There is also a striking immunological resemblance between both appendages, since the nail matrix, like the anagen hair bulb and the bulge, was shown to present unique characteristics of an immune privileged site. On the other hand, considerable progress in identifying nail stem cells has succeeded in locating putative stem cell niches in the nail unit. In this context, it is intriguing that nail stem cells residing in the nail matrix were recently shown to possess the ability to organize the process leading to digit regeneration. Further elucidation of signaling pathways governing epithelial–mesenchymal interactions in the nail unit seems to be a key to develop a novel therapeutic tool to treat amputees using nail epithelium. However, it is at least certain that the nail unit has a promising potential for the future of regenerative medicine. This review explores the biology of the nail organ by focusing on intriguing knowledge gained from recent studies.

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Contents

1. Introduction 000
2. Anatomy and histology of the human nail unit 000
2.1. Anatomy and histology of the nail unit 000
2.2. Origin of the nail plate 000
2.3. Comparison between human and mouse nail unit 000
3. Embryogenesis of the nail unit 000
4. Development, differentiation, and homeostasis of the nail unit 000
4.1. Dorsal–ventral determination 000
4.2. Factors relevant to nail development, differentiation, and homeostasis 000
4.3. Wnt signaling 000
4.4. Notch signaling 000
4.5. BMP signaling 000
4.6. Mesenchyme in the nail unit 000
5. Nail stem cells 000
6. Nail unit as a promising site for regenerative medicine 000
7. Immunology of the nail 000
8. Conclusion and future perspectives 000
References 000

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1. Introduction

The nail is a highly keratinized structure that grows on the dorsal tip of the digit. The nail corresponds to the hoof or claw of other vertebrates, and in higher primates, it has evolved along with the acquisition of manual dexterity [1]. For example, the human nail is considered to have various functions, including physical protection of the extremity, and assistance in fine manipulation and scratching. In dermatological practice, nail diseases are often difficult to diagnose and refractory to treatment, which may be partly attributed to insufficient pathophysiological understanding of the diseases. In the meantime, biological aspects of the nail apparatus have been characterized in recent years. Among others, there has been considerable progress in identifying nail stem cells and signaling pathways that regulate differentiation and homeostasis of the nail.

This review discusses, in addition to fundamental knowledge, recent advances in our understanding of biology and immunology of the nail unit. Furthermore, it introduces the latest finding that nail stem cells have a promising potential for regenerative medicine.

2. Anatomy and histology of the human nail unit

2.1. Anatomy and histology of the nail unit

It is essential to understand fundamental anatomy and histology of the nail unit for proper communication among clinicians and researchers (Fig. 1A and B). The primary components of the nail unit are the proximal nail fold (PNF), the nail matrix, the nail bed, and the hyponychium, together forming and supporting the nail plate, the keratinized structure which continuously grows throughout life [1,2].

Each component of the nail unit has specific histological characteristics [1,2]. Since the PNF is a wedge-shaped invagination of the skin on the dorsum of the digit, it has two surfaces that are histologically different. Its dorsal surface is a continuation of the digital skin with sweat glands, but no pilosebaceous units. On the other hand, its ventral surface has a quite thin epithelium without appendage and closely attaches to the dorsal surface of the nail plate. The cuticle is the stratum corneum of the tip and the ventral surface of the PNF, adhering to the dorsum of the nail plate.

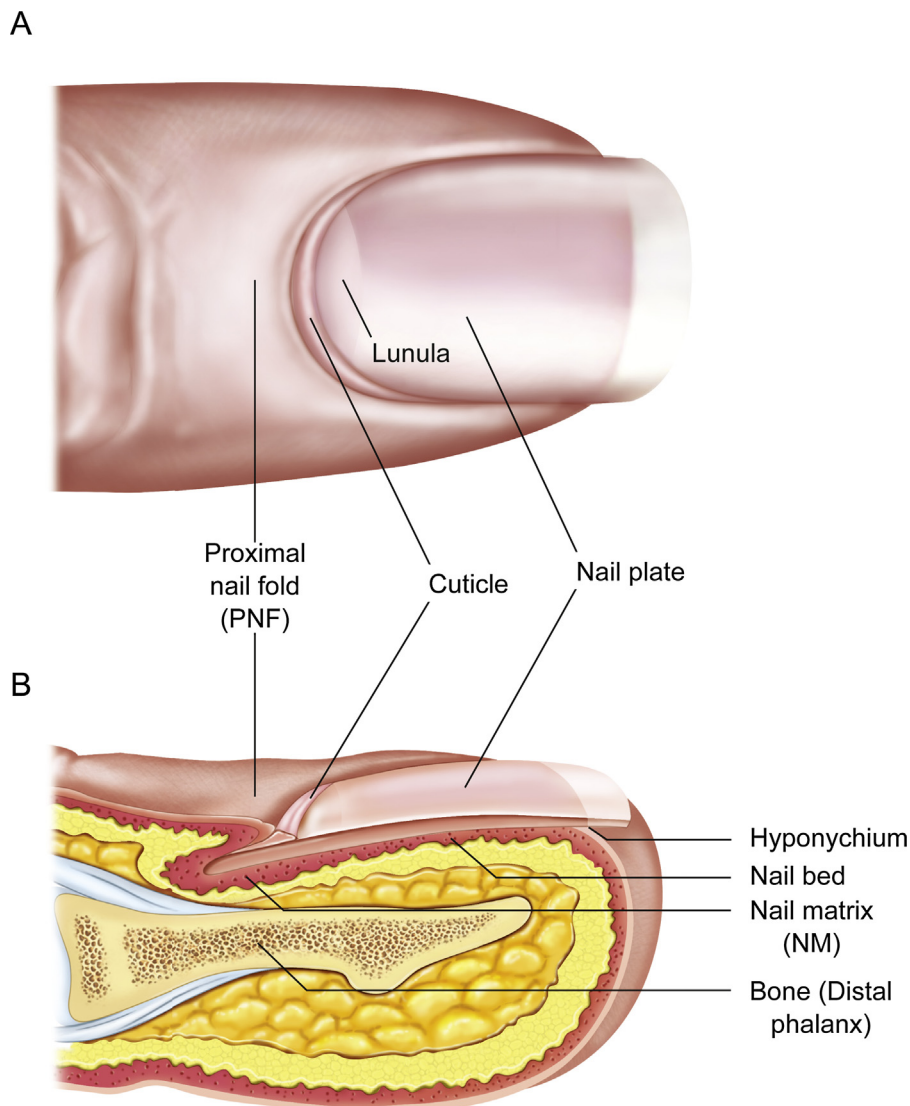


Fig. 1. Fundamental nail unit structure. (A) Diagram of the nail unit. (B) Diagram of a sagittal section through the nail unit.

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