



## Surfactant proteins: Role in lacrimal drainage disorders

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### ABSTRACT

Surfactants are complex mixtures of phospholipids and proteins produced by type II alveolar cells of the lungs and play a crucial role in pulmonary physiology. Six types of surfactant proteins (SP) are known; SP-A, SP-B, SP-C, SP-D, SP-G and SP-H. The major role of SP is in reducing surface tension and various immunological functions. SP-A, SP-B, SP-C and SP-D have been demonstrated in the tear film and the epithelium of the lacrimal sac (LS) and nasolacrimal ducts (NLD). All surfactant proteins except SP-G were also isolated from the canalicular tissues. The authors hypothesize that surfactant proteins play a significant role in the pathogenesis of lacrimal drainage disorders; functional nasolacrimal duct obstruction (FNLDO) and infective dacryocystitis.

### Introduction

Surfactants are complex mixtures of phospholipids and proteins produced by type II alveolar cells of the lungs and play a crucial role in pulmonary physiology [1]. Six types of surfactant proteins (SP) are known; SP-A, SP-B, SP-C, SP-D, SP-G and SP-H. While SP-B, SP-C and SP-G are known to reduce surface tension, SP-A, SP-D and SP-H are linked with immunological functions and mucosal defense mechanisms [1,2]. Extrapulmonary isolation of surfactants has been reported from oral cavity, brain, digestive system and testis [3–5]. SP-A, SP-B, SP-C and SP-D have been demonstrated in the tear film and the epithelium of the lacrimal sac (LS) and nasolacrimal ducts (NLD) [6,7]. All surfactant proteins except SP-G were also isolated from the canalicular tissues [8].

### Hypothesis

Surfactant proteins play a significant role in the pathogenesis of lacrimal drainage disorders; functional nasolacrimal duct obstruction (FNLDO) and infective dacryocystitis.

### Evaluation of hypothesis

Surfactant proteins B, C and G are small hydrophobic proteins which help in new lipid insertion into existing systems at air-fluid interfaces and contribute to lipid mono-layer stability [9]. This has a direct effect in reducing surface tension. The strong expression of SP-B and C in the canalicular system as well as the cytoplasm of the tall columnar epithelia of the lacrimal sac and nasolacrimal duct is not

without significance [6,7]. The tear fluid needs to pass smoothly and contiguously from the spread out large ocular surface into the narrow canaliculi with each blink. This would need a constant reduction of surface tension within the canaliculus to facilitate tear flow which is likely to be maintained and regulated by the canalicular surfactants. This would then allow tear fluid to pass in a continuous fashion and not as individual droplets. Similarly, the internal or luminal surfaces of the LS and NLD need reduction of the surface tension to allow regular tear flow. It is possible that the surfactant proteins isolated from the LS and NLD epithelia not only helps in tear flow but also regulate its rate of flow through the lacrimal drainage system (LDS). Taking these logical assumptions into consideration, a possible hypothesis on pathophysiology of functional epiphora or FNLDO can be formulated. It is possible that disorders of the surfactant proteins, either in the form of loss of synthesis, reduced production or structural alterations in the canaliculi and NLD may prevent smooth flow of tears through the LDS in spite of it being physically patent. This could then manifest as functional epiphora.

Surfactant proteins A, D and H modulate immune defenses via release of pro-inflammatory cytokines and reactive oxygen species. They also modulate phagocytosis and regulate opsonization process [10,11]. All these help in microbial clearance and possible mucosal defenses. SP-A knock out animal models have shown enhanced susceptibility to microbial infections [12]. Altered levels of SP-A and SP-D have been demonstrated in patients with periodontal infections and rhinosinusitis [13]. It can be hypothesized that the canalicular surfactants could be one amongst the first-line defenses against microbes which are washed from the ocular surface into the LDS. Similarly, during the entire course

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of tear flow till the nasal cavity, a constant effort would be needed by the LDS to maintain mucosal defenses against microbes, more so in narrow areas like NLD where greater tear stasis is expected. Surfactant proteins are likely to play a major role in this anti-microbial effort. Hence, it is possible that disorders of the surfactant proteins in the form of altered levels or reduced synthesis may enhance the susceptibility of an individual to acute infectious dacryocystitis.

### Current challenges and consequences of the hypothesis

Linking surfactant proteins to functional NLD obstruction and infective dacryocystitis would need extensive targeted investigations since the pathophysiology is multi-factorial. Site-specific molecular interactions of surfactants in LDS is yet to be ascertained. Animal experiments of the LDS involving surfactant knock out animal models would give insights into the clinical pathophysiology. The lead of surfactants in the etiopathogenesis of FNLDO and infective dacryocystitis is promising but may only partly explain the causative mechanisms involved unless all the interacting molecular pathways are deciphered. The discovery of these molecular mechanisms in FNLDO and infective dacryocystitis will have a massive impact on the way we treat them. It would not be audacious for us to believe that FNLDO would one day have a medical treatment and there may even be preventive strategies in the future.

### Conclusion

The presence of surfactant proteins in the LDS and their isolation from the canaliculus opens up exciting avenues to explore the pathogenesis of FNLDO and infective dacryocystitis.

### Conflict of interest statement

The authors report no conflict of interest.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2019.01.020>.

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