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SURFACTANT PROTEIN A AND D PERSONALIZED

MEDICINE: A HEALTHY DAY AT THE SP-A

To the Editor:

We thank Drs Guo and Krupnick, and Dr Lin, for starting the dialog with their commentaries. Lin says that apart from surfactant protein (SP)–A, steroids have multiple effects on cytokine production and so on. We would like to note that SP-A has been shown to affect proinflammatory cytokine production (tumor necrosis factor- α , interleukin [IL]-1 β , IL-6, IL-8, etc) in a dose dependent manner by either peripheral blood mononuclear cells or a macrophagelike cell line, and also that the human SP-A variants have been shown to differentially affect the production of cytokines. The levels of SP-A1 and SP-A2 are therefore very much relevant with regard to the expression of molecules that Lin considers important.

Moreover, SP-A has been shown to work through neutral factor- κ B-mediated mechanisms for modulating expression of cytokines. Recently, additional mechanisms have been identified through which SP-A1 and SP-A2 exert their differential effects.¹ Of relevance, infected mice that lack SP-A exhibit poor survival relative to wild-type mice,² and mice carrying different SP-A variants exhibit differences in survival and lung function.³ These and other pieces of information indicate the importance of SP-A in lung health.

Furthermore, the regulation of SP-A is complex and not fully understood at present, especially in the intact organ. The fact that different results were obtained in an established cell line versus lung explants, however, speaks to the fact that more work is needed to understand the differential regulation of SP-A variants in the intact lung under various experimental conditions, a point on which we are all in agreement. Moreover, the fact that a single-dose treatment of SP-A knockout mice with purified SP-A1 or SP-A2

and SP-A from human bronchoalveolar lavage samples resulted in increased survival of infected knockout mice³ and in a proteome profile of the alveolar macrophage similar to that in the wild-type mice further underscores the role of SP-A in lung health.

Given that innate immunity is the first line of defense, and that the innate immune SP-A and SP-D variants exhibit differences in survival and lung function under different experimental³ and clinical conditions,^{4,5} we postulate that even though the jury may be still out, it does seem to lean toward the importance of surfactant protein variants in lung health and potentially in playing a role in lung transplantation and the related pharmacogenetics, as we explored in the article published in this issue.

Joanna Floros, PhD^a

Frank D'Ovidio, MD, PhD^b

^aCenter for Host Defense, Inflammation, and Lung Disease (CHILD)

Research Department of Pediatrics

The Pennsylvania State University College of Medicine

Hershey, Pa

^bDivision of Thoracic Surgery

Columbia University Medical Center

New York, NY

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