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Compartment diversity in innate immune reprogramming

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1	Compartment diversity in innate immune reprogramming
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7	ABSTRACT
8	Pathogens or endogenous molecules can reprogram innate immunity. This process
9	can take the form of priming or tolerance depending on the activating signal, and
10	favors enhanced resistance of infection and other insults, by modulating
11	inflammation. Similarly to their organ-specific properties, reprogramming of
12	macrophages and NK cells, is also compartmentalized.
13	
14 15	Key words: BCG; β -glucan; cytokines; DAMPs; endotoxin; innate memory; PAMPs; zymosan.
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18	1. From endotoxin tolerance to innate immune reprogramming
19	Classically viewed as the first line of defense, cells of the innate immune system were
20	considered as early, non-specific and naïve responders. However, observations from the early
21	1940s suggested there might be more to the innate immune system than meets the eye. The
22	concept of endotoxin tolerance emerged in 1946, after Paul Beeson showed that repeated
23	injection of typhoid vaccine led to reduced fever in rabbits [1]. Reduced fever in response to
24	endotoxin (lipopolysaccharide, LPS) or killed bacteria as compared to controls was later
25	found in patients recovering from malaria [2], typhoid or paratyphoid fever [3] or with

26 pyelonephritis [4]. In the following decades, pre-treatment with endotoxin was shown to be

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