

Maternal Microchimerism in Renal Injury, Inflammation and Regeneration

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PURPOSE: Maternal microchimerism (MMc) acquired during pregnancy has been found in the blood and tissues of children, where it has been implicated in the pathogenesis of some autoimmune diseases. Increased levels of MMc in tissues have been found in patients with autoimmune diseases, but it is not known if these cells are specifically involved in the pathogenesis of autoimmune disease. Alternatively, maternal cells may proliferate or be recruited in response to non-specific inflammatory signals. In stem cell transplantation models, donor cells increase and differentiate within tissues during injury, inflammation and repair processes. We aim to test the hypothesis that MMc increases in response to organ-specific injury, inflammation, and regeneration in the absence of autoimmunity.

METHODS: Rhabdomyolysis with subsequent renal failure was induced in six-week old mice by intramuscular glycerol injection. Control mice were injected with saline. Renal injury, as monitored by plasma urea levels, occurred by 24 hours, was followed by acute inflammation, and resolved within 14 days. Full tubular regeneration occurred by day 28. MMc was detected by real-time quantitative PCR specific for the green fluorescent protein (GFP) gene in genomic DNA isolated from GFP^{-/-} progeny born to GFP^{+/-} females. Maternal cells in the progeny were characterized by immunofluorescence for GFP on frozen kidney tissue sections.

RESULTS: MMc was detected at an average level of 14 genome equivalents per 100,000 host cells (14 gEq/100K, SD 31) in 12 mice with renal failure compared to 44 gEq/100K (SD 115) in 12 controls. There was no significant difference in the frequency of MMc in treated mice compared to controls (54.5% vs. 41.6%). An increased frequency of MMc was detected during the inflammatory stage (day 7-14) in mice with renal failure (66.7%) compared to controls (16.6%). There was no correlation between levels or frequency of MMc and the severity of renal failure as determined by peak plasma urea levels. By immunofluorescence, maternal cells expressing GFP were detected in both injured and control kidneys and resembled hematopoietic cells and renal tubular epithelial cells.

CONCLUSIONS: MMc is common in the mouse kidney. There is no evidence that increased MMc is a general response to acute tissue injury and regeneration, although maternal cells may be involved in the acute inflammatory response. Consequently, increased MMc within tissues may be a phenomenon specific to autoimmune disease.