

Role of NLRP3 in an experimental model of testicular ischemia and reperfusion in mice

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Inflammasomes are multi-protein complexes composed of one of several leucine-rich repeat receptors (NLRs) including NLRP1, NLRP3, NLRC4 and AIM2: NLRP3 is currently the most fully characterized inflammasome. Testicular torsion leads to tissue degeneration and, after reperfusion, results in production of reactive oxygen species and triggers the apoptosis machinery. To better understand the role of NLRP3 during testicular ischemia/reperfusion (TI/R), we investigated the morphological aspects of spermatogenesis underlying the effects of inflammasome in KO mice during TI/R. KO (Nlrp3^{tm1bhk}) and wild-type (WT: C57Bl6) animals underwent 1h testicular-ischemia followed by reperfusion. The mice were killed after 1 day and 7 days of reperfusion and the determination of caspase-3 activity was executed. Furthermore, both the tubular (mean seminiferous tubule diameter and Johnsen's scoring system [1]) and extratubular (edema, hemorrhagic extravasation, vessels dilation, and Leydig cells changes [2]) compartments were evaluated. The TUNEL assay for apoptosis was also performed. After 1 and 7 days of reperfusion in WT mice an increase of caspase-3 was observed. Structurally, marked histological damages characterized by altered spermatogenesis, evident extratubular changes and increased TUNEL activity were observed. In KO mice caspase-3 was inhibited. Histological damages were significantly decreased, TUNEL activity was reduced and extratubular changes were significantly milder. We suggest that NLRP3 inhibition might have a protective role on spermatogenesis and it can be proposed in patients with unilateral testicular torsion.

References

- [1] Johnsen SG (1970) Testicular biopsy score count--a method for registration of spermatogenesis in human testes: normal values and results in 335 hypogonadal males. *Hormones* 1: 2-25.
- [2] Minutoli L et al. (2005) Evidence for a role of mitogen-activated protein kinase 3/mitogen-activated protein kinase in the development of testicular ischemia-reperfusion injury. *Biol Reprod* 73:730-736.

Keywords

Inflammasome NLRP3, seminiferous tubules, ischemia/reperfusion, caspase-3, TUNEL.