NLRP3 inflammasome involvement in the organ damage and impaired spermatogenesis induced by testicular ischemia and reperfusion in mice

L. Minutoli¹, P. Antonuccio², N. Irrera¹, M. Rinaldi¹, A. Bitto¹, H. Marini¹, G. Pizzino¹, C. Romeo², A. Pisani³, D. Puzzolo³, A. Micali³, F. Squadrito¹, D. Altavilla²

¹Dept. of Clinical and Experimental Medicine
²Dept. of Paediatric, Gynaecological, Microbiological and Biomedical Sciences
³Dept. of Biomedical Sciences and Morphofunctional Imaging, AOU Policlinico ‘G. Martino’, Via C. Valeria Gazzi, 98125 Messina, Italy

We investigated the role of NLRP3 inflammasome during testis ischemia and reperfusion injury (TI/R) in wild type (WT) and NLRP3 knock-out (KO) mice. WT and KO mice underwent 1 hour testicular-ischemia followed by 4 hours, 1 and 7 days of reperfusion or a sham TI/R. Furthermore, two groups of WT mice were treated, at the beginning of reperfusion and up to 7 days, with two inflammasome inhibitors, BAY 117082 (20mg/kg i.p.), or Brilliant Blue G (BBG; 45.5mg/kg i.p.) or vehicle. Animals were euthanized with a pentobarbital sodium overdose at 4 hours, 1 and 7 days and bilateral orchidectomies were performed. IL-1β and IL-18 mRNA, caspase-1 and -3 expression, TUNEL assay evaluation and a histological examination of spermatogenesis were carried out in all groups. TI/R in WT mice increased caspase-1 and IL-1β mRNA after 4 hours, and IL-18 mRNA at 1 day of reperfusion; there was also an increase in caspase-3 and in TUNEL-positive cells, a marked histological damage, and an altered spermatogenesis in WT mice in both testes after 1 and 7 days of reperfusion. KO TI/R mice, WT TI/R BAY 11-7082 and BBG treated mice showed reduced IL-1β and IL-18 mRNA expression, blunted caspase-1 and -3 expression, minor histological damages, low TUNEL activity and preserved spermatogenesis. These data suggest that the activation of NLRP3 plays a key role in TI/R and its inhibition might represent a therapeutic target for the management of patients with unilateral testicular torsion.