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SELECTIVE LYSINE SPECIFIC DEMETHYLASE 1 INHIBITOR, NCL1, COULD CAUSE TESTICULAR TOXICITY VIA THE REGULATION OF APOPTOSIS
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INTRODUCTION AND OBJECTIVE: Recent studies show that epigenetic alterations, such as lysine-specific demethylase 1 (LSD1), lead to oncogenic activation, suggesting such alterations as therapeutic target molecules. However, studies evaluating the effect of LSD1 inhibitors on male fertility are lacking. Here, we first analyzed the potential toxicity of new selective LSD1 inhibitor, NCL1, in the testis.

METHODS: Immunohistochemistry of LSD1 using human testicular samples was undertaken. Six-week-old male C57BL/6J mice were injected intraperitoneally with dimethyl sulfoxide vehicle, 1.0 mg/kg, 3.0 mg/kg NCL1-treated mice compared to control; cellular detachment, sloughing, vacuolization, eosinophilic changes and apoptosis. These results add to our knowledge of the effect of LSD1 inhibitors on male fertility.

RESULTS: In human samples, LSD1 was mainly expressed in Sertoli and germ cells, with intensity levels significantly decreasing in a progressively meiosis-dependent manner. Expression patterns among Sertoli and germ cells, with intensity levels significantly decreasing. NCL1 reduced the cell viability of GC-1, by apoptosis, but not TM3 and TM4 cell lines in a dose-dependent manner. Expression patterns among Sertoli and germ cells, with intensity levels significantly decreasing. Expression patterns among Sertoli and germ cells, with intensity levels significantly decreasing.

CONCLUSIONS: High-dose NCL1 targeting LSD1 caused dysfunctional spermatogenesis and induced caspase-dependent apoptosis. These results add to our knowledge of the effect of LSD1 inhibitors on male fertility.