

Journal of Andrology, Vol 17, Issue 3 249-255, Copyright © 1996 by The American Society of Andrology

JOURNAL ARTICLE

Effect of chloroquine on the formation of tight junctions in cultured immature rat Sertoli cells

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Adjoining immature Sertoli cells in the seminiferous epithelium form a tight junctional complex leading to the development of the blood-testis barrier. Protease and antiprotease activities have been implicated in the process of formation of tight junctions. Here, we report the effect of chloroquine, an antimalarial drug with antiprotease activity, on the development of intercellular tight junctions in cultured immature rat Sertoli cells. For positive control, the classical lysosomotropic agent ammonium chloride was used. Sertoli cells were seeded in serum-free defined medium at a density of 3×10^6 cells/0.64-cm² well on Matrigel-covered Millicell-HA filters. Chloroquine at concentrations ranging from 25 to 100 μM was added to the outer chamber of the bicameral system on either day 1 or 7 of the culture. The formation of the tight junction was monitored by the measurement of the transepithelial resistance (TER) at 24-hour intervals using an impedance meter. TER in untreated controls was 50 ohms/cm² on day 1; it increased progressively to 80 ohms/cm² by day 7 and plateaued until day 12. The cells treated from day 1 with chloroquine also showed a dose-dependent progressive increase in TER until day 9, reaching 225 ohms/cm² in cells treated with the 100 μM concentration. In comparison to controls, the increase in TER was significantly higher. In cells treated with chloroquine starting from day 7 of culture onwards, there was no observable difference in TER from the untreated control. These observations demonstrate that chloroquine and ammonium chloride increase the TER of immature Sertoli cells in the bicameral chamber.

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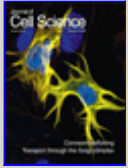
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