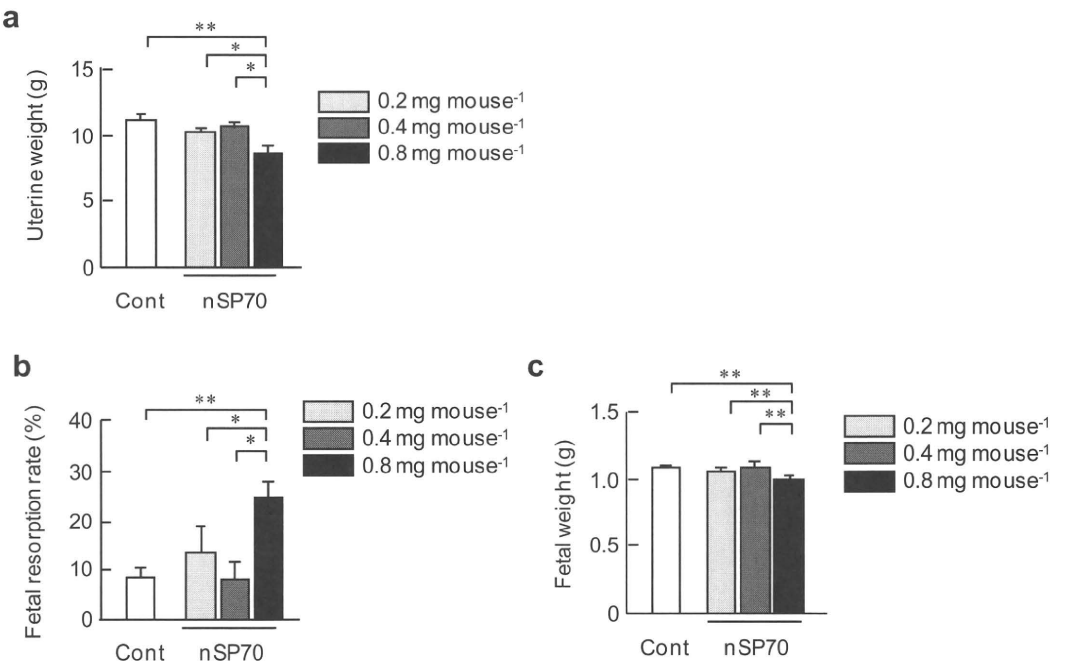

Figure 1. Dose-dependent toxicity of nSP70. Pregnant BALB/c mice were treated with 100 μl of 0.2, 0.4, or 0.8 mg/mouse nSP70 or PBS (control) intravenously *via* tail vein on two consecutive days, at GD16 and GD17. At GD18, uterine weights (a), fetal resorption rates (b), and fetal weights (c) were evaluated. All data represent means ± SEM. ($^{*}P < 0.05$, $^{**}P < 0.01$)

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Reduced Stathmin-1 Expression in Natural Killer Cells Associated with Spontaneous Abortion

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Female CBA/J mice impregnated by male DBA/2J mice (CBA/J×DBA/2J matings) are prone to spontaneous abortion, although the reason for this is unclear. In this study, the stathmin-1 expression pattern was evaluated in uterine natural killer (uNK) cells purified from CBA/J×DBA/2J matings. Results were compared with those in a CBA/J×BALB/c control group that yields successful pregnancies. The mean ± SD percentage of stathmin-1$^+$ cells in the CD49b$^+$ uNK cell population was lower in CBA/J×DBA/2J mice (0.7% ± 0.4%) than in control CBA/J×BALB/c mice (4.9% ± 1.5%, $P < 0.01$) using flow cytometry, and the intracellular stathmin-1 level in uNK cells was lower in CBA/J×DBA/2J mice than in control mice using Western blot analysis. Co-localization of lectin from Dolichos biflorus agglutinin (DBA-lectin) and stathmin-1 was confirmed using multivision immunohistochemical analysis. The frequency of stathmin-1$^+$DBA-lectin$^+$ cells was lower in CBA/J×DBA/2J mice than in CBA/J×BALB/c mice. A similar trend in the frequency of stathmin-1$^+$CD56$^+$ cells was seen in patients with unexplained spontaneous abortion compared with normal early pregnancy. A neutralizing antibody against stathmin-1 further increased the percentage of embryo loss in CBA/J×DBA/2J matings. These results provide evidence that stathmin-1 expression in uNK cells at the maternal-fetal interface may help modulate uNK cell function and may be beneficial for a successful pregnancy. *(Am J Pathol 2011, 178:506–514; DOI: 10.1016/j.ajpath.2010.10.005)*

Stathmin-1 is a small (19-kDa) regulatory phosphoprotein that integrates diverse intracellular signaling pathways. It is highly conserved among vertebrates and is associated with tubulin binding and microtubule destabilization.[1,2] Stathmin-1 has a complex phosphorylation pattern in response to various extracellular signals, in particular growth and differentiation factors.[3] Moreover, stathmin-1 phosphorylation varies during the cell cycle.[4] It has thus been thought that stathmin-1 can act as a relay integrating the activation of diverse intracellular signaling pathways and mediating the control of cell proliferation, differentiation, and other functions.[5]

Stathmin-1 protein and mRNA were previously shown to be expressed in the pregnant uterus and decidualizing endometrial stromal cells in human and murine models.[6–8] Furthermore, stathmin-1 is up-regulated in rodent uteri at the site of embryo implantation and is highly

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