Pig as an experimental model for in vitro and in vivo studies of radiosensitivity of B lymphocytes and NK cell

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Introduction: Lymphocyte subsets differ in their susceptibility to ionizing radiation. B cells are more radiosensitive than major (CD4+CD8- and CD4-CD8+) T cell subsets; results on radiation-induced NK cell apoptosis are controversial. Most data come either from experiments in vitro or examinations upon accidental irradiation with ill-defined doses. In vivo models include laboratory rodents and a large animal model is missing. Here we show that pigs represent a convenient model for in vitro and vivo studies of radiosensitivity of B lymphocytes subsets with possible implications in biodosimetry. Methods: Doses in the range of 1-8 Gy were used for whole body irradiation of one-month-old boars. Heparinized blood was collected before irradiation (control), immediately after irradiation and after selected time intervals (up to 48 hr). Samples were analyzed immediately after collection or upon 6 - 48 hr cultivation. Total leukocyte counts and relative numbers of lymphocyte subsets were analyzed by immunophenotyping and multicolor flow cytometry. Results: As expected, total leukocytes counts decreased with a dose and time both in vivo and in vitro. Similar to humans and rodents, B cells represented the most sensitive lymphocyte population. The comparison of individual B cell subsets has revealed that the CD2- subset is less prone to radiation induced apoptosis than CD2+ B cells. In the T cell compartment, CD4+CD8- cells are more radioresistant than their CD4-CD8+ counterparts. Among CD4+ T cell subsets, the double positive (CD4+CD8+) population and cells with surface CD25 expression belong to the most radioresistant ones. Importantly, while the CD8+ NK population (CD3-CD8+ lymphocytes) rapidly disappears after irradiation both in vitro and in vivo, such cells re-appeared circulation as soon as 24 hr after irradiation with lower doses. Conclusions: Short term (6-24 hr) cultivation of full blood collected from irradiated individuals represents a convenient and reliable approach for in vivo studies on ionizing radiation induced apoptosis of lymphocyte subsets in vivo. B and NK subsets have been proved as useful biomarkers of the received dose. Different radiosensitivity of NK cells and their precursors is suggested as the reason of formerly published discrepancies in NK cells radiosensitivity. Acknowledgement: Supported by projects of the Ministry of Defence of the CR OPUOFVZ200604 and Ministry of Education,Youth and Sports No. 2B08028.