

SURVIVAL AND CHROMOSOME INJURY OF SPHEROID CELLS AFTER IRRADIATION

H. DERTINGER*, D. HOLSER**, G. HINZ*

*Kernforschungszentrum Karlsruhe, Institut für Genetik und für
Toxikologie von Spaltstoffen, Karlsruhe

**Biologisches Institut der Universität Stuttgart

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Multicell spheroids (SPH) offer unique advantages for studying modifications of single cell radiosensitivity due to the extensive intercellular communication in a three-dimensionally organized tissue. We have been able to relate the increased radio-resistance of spheroid cells as compared to monolayer (ML) cells ("Contact Resistance") to the degree of ionic coupling between the cells as measured by a micro-electrode technique /1/. The coupling strength was expressed as R_0/R_c where R_0 and R_c are the electrical membrane resistances of isolated cells or cells within a monolayer, respectively. Table 1 summarizes the results obtained for six different cell lines. Whereas L, Hela and V79 cells are only weakly coupled, 3T3, B14 and BICR show a pronounced decrease in R_c due to intercellular conductance. Contact resistance (CR) was determined from the survival curves of SPH and ML cells after γ -irradiation and expressed as the dose ratio (SPH/ML) for 50 % survival (r_{50}). Table 1 shows r_{50} to increase with increasing coupling (R_0/R_c) suggesting a correlation between CR and coupling. Table 2 shows that CR considerably reduces the rate of chromosome damage in SPH of B14 cells. Even the quality of chromosome damage is different in both systems. There is no doubt that CR is a significant parameter for radiation therapy and -carcinogenesis though the interrelation between cell coupling and the expression of genetic and lethal damage is not yet fully understood.

Table 1 Coupling strength R_o/R_c and Contact Resistance r_{50} (see text for explanations) for 6 cell lines. SPH diameter: 250 μm ; ML cell density: $3 \cdot 10^4 \text{ cm}^{-2}$; Irradiation: Co- γ /37 C; Absolute membrane resistances: 2-20 M Ω ; Medium: Eagle MEM/15 % FCS + Antibiotics.

Cell Line	Origin	R_o/R_c	r_{50}
L	Mouse	0.98	1.00
HELA	Human	1.08	1.16
V79	Chin. Hamster	1.21	1.22
3T3	Mouse	1.71	1.88
B14 F28/B7	Chin. Hamster	2.04	2.92
BICR/MIR-K	Rat	4.50	3.01

Table 2 Chromatid-type aberrations in B14 F28 cells; Dose: 5 Gy (Co-Gamma)

	Monolayer	Spheroid
Mean number of aberrations per cell	2	0.2
Exchanges (%)	36	0
Breaks (%)	35	32
Gaps (%)	29	68
Cells without aberrations (%)	16	78
Viable cells (colony formers) (%)	35	80

References: /1/ Hülser, D., and Webb, D., *Exptl. Cell Res.* 80 (1973) 210.