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Cytological and Cytogenetical Studies on Brain Tumors

IV. Identification of the Missing G Chromosome in Human Meningiomas as No. 22 by Fluorescence Technique*

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Summary. In human meningiomas one G group chromosome is regularly missing. Using a fluorescence staining (Atebrine-acetic acid) in 5 meningiomas it could be shown that always one chromosome No. 22 was missing. In one meningioma we found an accessory stemline bearing a Ph^1-like chromosome, which could be identified to be a deleted No. 22. — The similarities of the chromosomal findings in meningiomas and the chronic myeloic leukemia are discussed.

Zusammenfassung. Als regelmäßiger Befund ist beim menschlichen Meningeom der Verlust eines G-Chromosoms nachzuweisen. Wir untersuchten mit Hilfe einer Fluorescenzfärbung (Atebrin-Essigsäure) 5 Meningeome und konnten zeigen, daß immer ein Chromosom Nr. 22 fehlt. In einem Meningeom, das eine zusätzliche Stammlinie mit einem Ph^1-ähnlichen Chromosom aufweist, wurde das Fragment als deletiertes Chromosom Nr. 22 identifiziert. — Die Ähnlichkeit der chromosomen-morphologischen Befunde beim Meningeom und bei der chronischen myeloischen Leukämie werden diskutiert.

As already reported, in human meningiomas one G chromosome is regularly missing (Zang and Singer, 1967, 1968; Singer and Zang, 1970; Porter *et al.*, 1969; Mark, 1970). But until now it is unknown whether always the same chromosome has been lost. The fluorescence method of Caspersson *et al.* (1970a) made it possible to answer this question, because he found different fluorescence patterns in the 2 pairs of the G group chromosomes.

For our investigations we used a modification of Caspersson's method described recently by Kim *et al.* (1971). Due to the low mitotic index of meningiomas the biopsies were cultured for 3—7 days. Chromosome preparations were done directly on cover slips without trypsinization (for details see Singer and Zang, 1970; Kersting, 1961). The cover slips were transferred from absolute alcohol through an alcohol series and aqua dest. into 1—2% acetic acid. We stained in a solution of 0.5% Atebrine (Gurr) in 2% acetic acid for 5 min (pH 3—4). The lamellae were rinsed two times with aqua dest., mounted cell side down onto a slide with some drops of distilled water and sealed with nail polish. The chromosomes were analyzed under incident light (Leitz Orthoplan microscope, vertical Opak-illuminator, 100 plan-apochromatic oil immersion objective, Xenon-150-lamp, 5 mm BG 12 excitor filter, 510 mm barrier filter). From each of the 5 meningiomas studied up to now by this method about 20 well spread mitoses with long stretched chromosomes were photographed. The staining technique of Kim *et al.* produced a distinct fluorescence pattern, showing no difference to chromosomes stained

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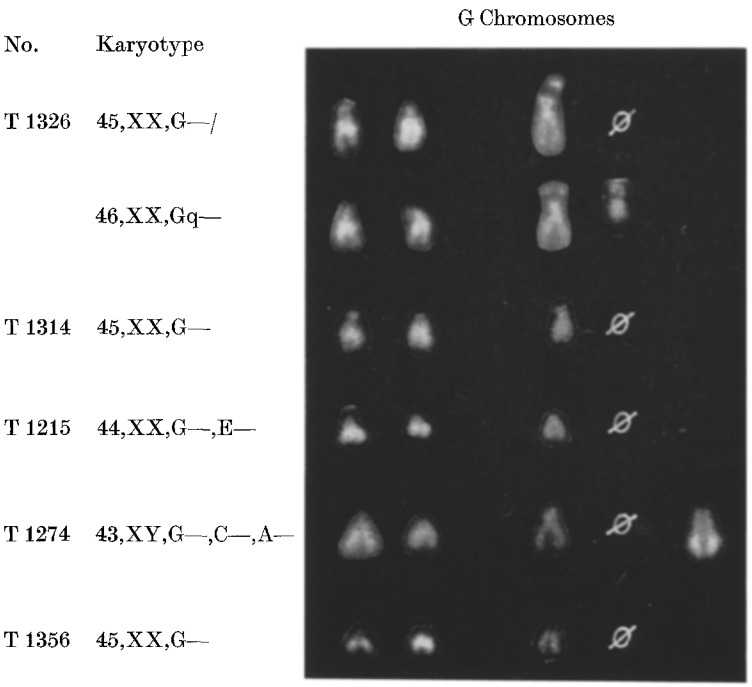

Fig. 1. Differentiation of the G group chromosomes in meningiomas by fluorescence staining: No. 21 shows a brightly fluorescenting band on the middle part of the long arm; No. 22 shows a uniform weak fluorescence over the whole long arm and occasionally a bright band on the short arm. It is mostly longer than No. 21 but seems to differ in size, depending on the fluorescence intensity. Always one chromosome No. 22 is missing (or deleted)

by quinacrine mustard, but stable enough to use a 100 ASA film (Ilford FP 4). Beside the fluorescence investigation the karyotypes of the meningiomas were established by examination of about 30 mitoses photographed with usual Orcein staining.

After fluorescence staining in 3 tumors the chromosome No. 22 seemed to be significantly longer than No. 21 (Fig. 1). As this difference is less distinct in Orcein stained chromosomes, we believe it to be enhanced by the fact that No. 21 shows only a strong fluorescenting band in the middle part of the long arm whereas No. 22 is weakly fluorescenting over its whole length.

The *results* are summarized in Fig. 1. In all of the 5 meningiomas always one of the weaker fluorescenting G chromosomes was missing, classified by Caspersson to be No. 22, although it seems to be the longer one. Because of the good agreement within our results we assume that in meningiomas regularly one chromosome No. 22 has been lost. As Caspersson *et al.* (1970b) reported the Ph^1-chromosome in chronic myeloic leukemia to be a deleted chromosome No. 22 the cytogenetic similarity between the meningiomas and this leukemia is remarkable. It becomes still more obvious since we detected a Ph^1-like chromosome deletion in 5 tumors of our series of more than 70 meningiomas (Zankl and Zang, 1971). Furthermore by chance one of the meningiomas examined by fluorescence technique showed a side line with a Ph^1-like chromosome, identifiable also as a deleted No. 22 (Fig. 1).

These new facts support our assumption about some analogies in the nature of origin of the chronic myeloid leukemia and the meningiomas, mentioned already

before (Zankl and Zang, 1971). Therefore we like to discuss that the distal part of the long arm of chromosome No. 22 bears genetic information involved in the control of cell proliferation. On the one hand the loss of genetic material at this site might enhance the cell proliferation directly or by triggering further chromosome disturbances. On the other hand a Ph^1-like deletion of chromosome No. 22 could indirectly predispose cells to tumorigenic influences.

References

Caspersson, T., Zech, L., Johansson, C., Modest, E. J.: Identification of human chromosomes by DNA-binding fluorescent agents. Chromosoma (Berl.) **30**, 215—227 (1970a).

— Gahrton, G., Lindsten, J., Zech, L.: Identification of the Philadelphia chromosome as a number 22 by quinacrine mustard fluorescence analysis. Exp. Cell Res. **63**, 238—240 (1970b).

Kersting, G.: Die Gewebszüchtung menschlicher Hirngeschwülste. Berlin-Göttingen-Heidelberg: Springer 1961.

Kim, A., Bier, L., Majewski, F., Pfeiffer, R. A.: Fluorochromierung menschlicher Chromosomen mit Atebrin-Essigsäure. Humangenetik **12**, 257—260 (1971).

Mark, J.: Chromosomal patterns in human meningiomas. Europ. J. Cancer **6**, 489—498 (1970).

Porter, I. H., William, F. B., Brown, C. D., Paul, G.: Recent advances in molecular pathology: Some aspects of chromosome changes in cancer. Exp. molec. Path. **11**, 340—367 (1969).

Singer, H., Zang, K. D.: Cytologische und cytogenetische Untersuchungen an Hirntumoren. I. Die Chromosomenpathologie des menschlichen Meningeoms. Humangenetik **9**, 172—184 (1970).

Zang, K. D., Singer, H.: Chromosomal constitution of meningiomas. Nature (Lond.) **216**, 84—85 (1967).

— — The cytogenetics of human tumors. Angew. Chemie Internat. Edit. **7**, 709—718 (1968).

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