

## ARE MONOSOMIES UNDERESTIMATED WHILE ANALYZING CANCER CELLS?

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Since the beginning of the 20<sup>th</sup> century, it is known that aneuploidies play a role in cancer. Lots of chromosome abnormalities both numerical and structural are very common in cancer cells and this marked genomic instability is a hallmark of cancer [1, 2]. Mechanisms that cause aneuploidy produce monosomies as well as trisomies. Yet, when the literature on cancer cytogenetics is scanned, it is seen that most of the papers — especially on hematologic cancers — discuss only the structural abnormalities or trisomies, whereas only a minority of them reports monosomies at all. I find this quite surprising, because our own experience shows that clonal monosomies are quite common in cancer cells.

Of course there is a difficulty in interpreting monosomies in classical cytogenetics because of the risk of “creating” them in the process of slide making. Just because of this reason, in ISCN (1995/2005) [3, 4] a more strict criterion is approved for monosomies; while trisomies and structural abnormalities are accepted clonal if they are present in two metaphases, monosomies must exist in at least three cells. Therefore, when a clonal monosomy is observed, it must have drawn attention as much as a clonal trisomy or structural abnormality. But usually clonal monosomies are not discussed and left hidden in karyotype formulas especially if they are not reported by other papers before.

When I consider our own — relatively-high monosomy rate in cancer cells, I cannot be convinced that all our monosomies are the results of technical errors in slide making. We observe quite a lot clonal monosomies in different tissues and different cancer types (blood, marrow and solid tumor tissues like lung and brain cancers). However, we do not see them in slides prepared from blood cultures of the patients without cancer. Even if we occasionally find a random monosomy in such cases, they never reach the stage of clonality.

The papers that concern monosomies are usually on FISH experiments with the probes of few known monosomies like-7 or sex chromosome monosomies. Although these works are important and necessary, this approach only confirms already known results and do not add new monosomies on the list.

There are some papers that although they do not mention in their discussions, they have some clonal monosomies in tables which contain karyotype formulas (exemplary references [5–7]). But some authors do not put tables of the karyotype formulas into their papers

at all, and this is a pity because there is no way to know whether they had observed any monosomy or other abnormality that they consider unworthy to mention. It can be thought that to observe a clonal monosomy in only one case's sample, it is not worth discussing. But again it is important to put them in the karyotype lists at least, so that it can be possible to collect data from literature.

It will be necessary to confirm the classical cytogenetics results with FISH analyses, but to come to that point, we must report and discuss these findings at first in classical cytogenetics reports. It is all natural to expect monosomies in cancers because there is a very wide literature on the loss of heterozygosity (LOH) in cancers and monosomy is a mechanism of LOH. On the contrary, the current situation (not discussing monosomies in cancer papers) seems very odd in this context. Furthermore, it is all in accordance with the concept of aneuploidies being the primary cause of cancer [8].

It is only understandable that the authors prefer to emphasize the structural abnormalities and trisomies rather than monosomies to evade being criticized as being erroneous in their slide making. But I think that we must be more courageous to report clonal monosomies, because, the false positive ones will eventually be eliminated as being not reported by other papers, therefore, not confirmed. But the ones that are reported by several groups will be great contributions to the data pool on the subject.

### REFERENCES

1. Heim S, Mitelman F. Cancer cytogenetics, 3rd ed. New York: Wiley-Liss, 2009. 736 p.
2. Miller OJ, Therman E. Human chromosomes, 4th ed. New York: Springer, 2001. 501 p.
3. Mitelman F, ed. ISCN: an international system for human cytogenetic nomenclature. Basel: S Karger, 1995. 114 p.
4. Shaffer LG, Tommerup N, eds. ISCN: an international system for human cytogenetic nomenclature. Basel: S Karger, 2005. 130 p.
5. Babicka L, Zemanova Z, Pavlistova L, et al. Complex chromosomal rearrangements in patients with chronic myeloid leukemia. *Cancer Genet Cytogenet* 2006; **168**: 22–9.
6. Miura I, Siegfried JM, Resau J, et al. Chromosome alterations in 21 non-small cell lung carcinomas. *Genes Chromosomes Cancer* 1990; **2**: 328–38.
7. O'Dwyer ME, Gatter KM, Loriaux M, et al. Demonstration of Philadelphia chromosome negative abnormal clones in patients with chronic myelogenous leukemia during major cytogenetic responses induced by imatinib mesylate. *Leukemia* 2003; **17**: 481–7.
8. Duesberg P, Li R, Rasnick D, et al. Aneuploidy precedes and segregates with chemical carcinogenesis. *Cancer Genet Cytogenet* 2000; **119**: 83–93.

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