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This Week's Citation Classic

Arrighi F E & Hsu T C. Localization of heterochromatin in human chromosomes. *Cytogenetics* **10**:81-6, 1971. [Dept. Biology, M.D. Anderson Hosp. and Tumor Inst., and Grad. Sch. Biomedical Sciences, Univ. Texas, Houston, TX]

Differentially stained chromosome areas can be obtained by subjecting cytological preparations to C banding procedures. The darkly stained areas are heterochromatin, which is composed of repeated DNA sequences. These sequences may be heterogeneous and of varying length. [The *SCI*® indicates that this paper has been cited in over 810 publications since 1971.]

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"The development of cytology into the cytogenetics that we know had a beginning, at least, in the last century. A recent highlight in this development was the successful *in situ* hybridization experiments of Pardue and Call in 1969.[1] From their technique, the chromosome banding techniques developed that gave biologists insight into chromosome structure that was not previously possible. After learning the *in situ* hybridization technique in the laboratory of J.G. Gall, I returned to Houston to attempt to confirm their work with the mouse satellite DNA and to do other studies. Collaboration with Priscilla and Grady Saunders began. We spent considerable time isolating total and satellite DNA from mouse liver and then lost the satellite DNA. After discussing this discouraging event with Grady Saunders, we decided to try *in situ* hybridization on human DNA using repeated DNA sequences obtained by reassociation at various Cot values as the mobile component. We observed in these experiments that chromosomes had differentially stained areas and that these stained areas[2,3] also were composed of repeated sequences like those for the mouse reported by Pardue and Gall.[1] This subsequently led us to use portions of the *in situ* hybridization procedure on cells from a number of species, including rodents, bats, hoofed animals, carnivores, primates, and human beings. At the International Congress of Human Genetics in 1971, following the Paris Chromosome Standardization Conference, we reported that a satellite DNA from human cells had hybridized to the heterochromatin of human chromosome 9.[4]

"The development of these techniques has had a profound impact on diagnostic cytogenetics and the interpretation *of* chromosome evolution among species. Specific chromosome changes associated with congenital abnormalities and diseases can be assessed using Q, C, R, or C banding procedures. However, the function of heterochromatin and its cellular role is still unclear.

"We realized the potential usefulness of this procedure in biology and medicine, but the first journal to which the paper was submitted rejected it on the grounds that the work had no medical application. That this research work and technique have wide use and peer acceptance is a major satisfaction for us.

"These studies were completed when application for funding for basic research did not take so much time out of our day and therefore we had more time for scientific creativeness."

1. **Pardue M L & Gall J G**. Chromosomal localization of mouse satellite DNA. *Science* **168:**1356-8, 1970.
2. **Arrighi F E, Saunders P, Saunders G F & Hsu T C**. Distribution of repetitious DNA in human chromosomes. *Experientia* **27**:964-6, 1971.
3. **Hsu T** C, **Arrighi F E & Saunders** G F. Compositional heterogeneity of human heterochromatin. *Proc. Nat. Acad. Sci. US* **69**:1464-6, 1972.
4. **Arrighi F E, Getr M J, Saunders G F, Saunders P & Hsu T C.** Location of various families of human DNA on human chromosomes, (de Grouchy J, Ebling F J G, Henderson I & Franqois J, eds.) *4th International Congress of Human Genetics, Paris, 6-11 September 1971. Abstracts of papers presented.* Amsterdam: Excerpta Medica, 1971. p. 18.