Abstract Title: Multilayer organization of chromosomes and its implications in cytogenetics

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Abstract: Early electron microscopy studies showed that mitotic chromosomes swollen with water have a fibrillar morphology and since then most structural models consider that chromosomes are formed by chromatin fibers folded into loops. However, under metaphase ionic conditions, cryo-electron tomography showed that chromatin emanated from chromosomes is planar and forms multilayered plates. The small thickness of the layers (approx. 6 nm) suggested that they are monolayers of nucleosomes slightly tilted relative to the plate surface. These observations and previous electron microscopy and atomic force microscopy studies led us to the proposal of the thin-plate model consisting of many chromatin layers stacked along the chromosome axis (in human chromosomes each layer contains approx. 0.5 Mb of DNA). On the other hand, banded karyotypes and multicolor cytogenetic analyses provide structural information: (i) chromosome bands and the connection surfaces in sister chromatid exchanges and in translocations are planar and orthogonal to the chromosome axis, (ii) chromosome stretching causes band splitting, and (iii) even the thinnest bands (approx. 1 Mb) are orthogonal and well defined. The thin-plate model is the only proposed structure that is compatible with the orthogonal orientation and planar geometry of the connection surfaces in chromosome rearrangements; it is also compatible with the observed orientation of bands, with the existence of thin bands, and with band splitting. Furthermore, microdissection-based multicolor banding experiments showed that chromosome bands are maintained during interphase. This could be related with our results indicating that chromatin emanated from G1, S, and G2 nuclei also has a plate-like morphology but shows a low tendency to form multilayered structures. It is hypothesized that the tight layer stacking in mitosis inhibits transcription but, in interphase, specific clusters of layers are unstacked in different cell types and DNA can interact with the proteins of the transcriptional machinery to activate gene expression.

Area of expertise: Chromatin and chromosome structure.