A Novel Class of Molecular Probes for Cellular Imaging

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Nowadays, there are several probes to increase contrast in cellular imaging for confocal or electron microscopy. However, the majority of these probes often lack contrast for both microscopic technique or specificity for the target. Few probes display both microscopic techniques, yet they may hinder cell functions due to their size. Organometallic probes are engineered with nanoscopic design, specific targeting moieties to minimise the impact on cell function, and compatibility for light and electron microscopy. Organometals offer the outstanding advantage of owning high electron density due to their metal core. The metal core of the probe is usually made by elements which do not belong to cells. Thus, this peculiarity may offer the possibility to analyse the elemental composition of the specimen through energy-filtered transmission electron microscopy (EF-TEM) to further characterise the target of interest within the cell. Ir-Tub is a cyclometalated Iridium (III) complex, which intercalates between the subunit a and b of microtubulin, a critical component of the cell cytoskeleton. After treatment with Ir-Tub, microtubules in HepG2 cell were analysed by EF-TEM using a JEM2200 equipped with cold field emission gun (FEG) and W filter (figure 1). The binding site spacing of Ir-Tub, determined from the Ir chemical map, via the signal from the organometal is in very good agreement with the in silico model (figure 1c-e).[1] Organometallic probes are beginning to prove their unique properties as contrast providing agents for microscopic techniques such as confocal microscopy, TEM and EF-TEM, and liquid-phase TEM. Hence, compared to other labelling agents, organometallic compounds represent a new class of microscopic probes for investigating and understanding the mechanisms involved in cellular processes.

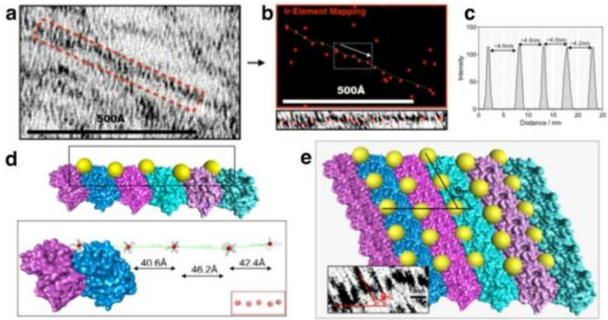

Figure 1. TEM evaluation of an organometallic probe (Ir-Tub) for microtubules on treated HepG2 cells. (a) Magnified image of a microtubule in the cell. (b) Iridium elemental map achieved in EF-TEM mode and (below) its superimposition with the TEM image, displaying how Ir-Tub complexes intercalate within microtubules stripes. (c) Distance measurement of neighboured Iridium elements, and (d) the comparison with the measured distance from the computational model. (d) Angle measurement of neighboured microtubules stripes with its horizontal line as polar coordinate system (θ_{tb}=68°), and similar measurement from polymerized microtubule model (θ_{md}= 68°).[1]

References

[1] Tian, X., <u>De Pace, C</u>., Ruiz-Perez, L., Chen, B., Su, R., Zhang, M., Zhang, R., Zhang, Q., Wang, Q., Zhou, H., Wu, J., Battaglia, G., Zhang, Z. & Tian, Y. An Organometallic Ir (III) Molecular Probe for Imaging Microtubules in Fluorescence and Electron Microscopy. *bioRxiv* (2018). DOI: 10.1101/351098