A significant advantage of using tubulins from HeLa or MCF-7 cell lines over neuronal tubulins is that they are derived from actively dividing human cancer cells and are thus more appropriate model systems for cancer research. Tubulins from different tissue vary in the relative abundance of specific isoforms and the nature of post-translational modifications. These tissue type specific variants of tubulin have different biological and biochemical properties. It follows that the development of anti-tubulin ligands would benefit from the use of tubulin species purified from tissues that are relevant to the pathology under investigation. The specificity of ligands for a particular tubulin variant can be determined by performing comparative studies with both cancer cell and neuronal tubulins. We have advanced this concept by developing the Tubulin Ligand Index (TLI) system (Davis et al. 2009). In this system, IC50 values for inhibitory compounds or EC50 values for stabilizing molecules are determined in polymerization assays using cancer cell and neuronal tubulins. The IC50 or EC50 values for each tubulin variant are analyzed as a ratio (neuronal/cancer cell) and allow for determinations of the relative specificity for each tested compound. TLI values greater than 1.0 indicate that a particular compound is more active on cancer cell tubulin. Conversely, TLI values less than 1.0 suggest that a compound is more specific for neuronal tubulin. Table 1 and II summarize data (HeLa and MCF-7 resp.) from a study comparing the specificity of several tubulin ligands using the TLI system.

Table I - Summary of TLI values for HeLa versus Neuronal tubulin

Compound	$IC50_{neuronal}$	$IC50_{HeLa}$	$TLI_{(neuronal/HeLa)}$
Nocodazole	3.4	3.2	1.06
Mebendazole	4.0	25	0.16
Paclitaxel	0.48	1.04	0.46
Vinblastine	1.10	2.83	0.39

Footnote:

1. All values in micromolar drug concentration.

2. All IC50s have errors of +/ -50%.

Figure 1: Example polymerization curves for HeLa cell tubulin (Cat. # H001)

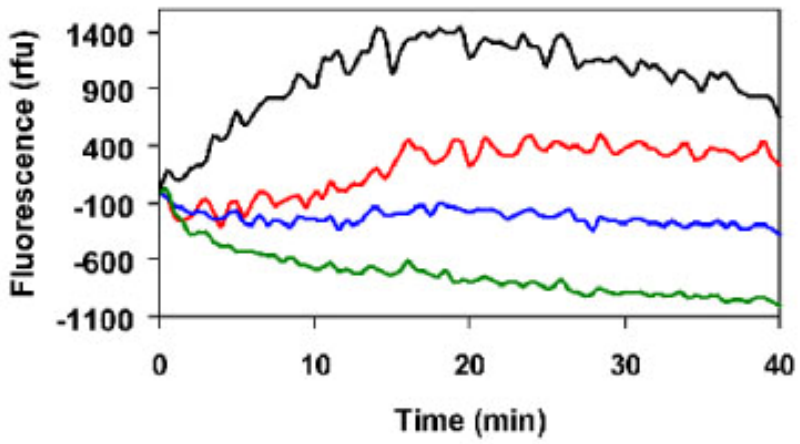


Table II - Summary of TLI values for MCF-7 versus Neuronal tubulin

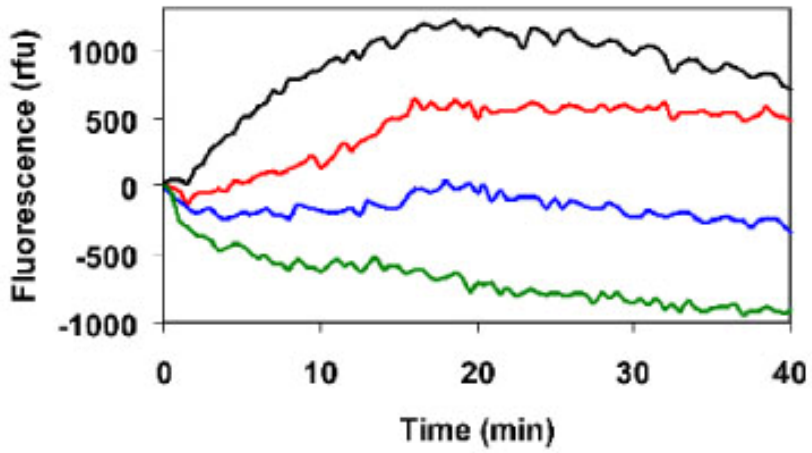
Compound	$IC50_{neuronal}$	$IC50_{MCF-7}$	$TLI_{(neuronal/MCF-7)}$
Nocodazole	3.4	3.2	1.06
Mebendazole	4.0	14.8	0.27
Paclitaxel	0.48	0.51	0.94
Vinblastine	1.10	1.21	0.91

Footnote:

1. All values in micromolar drug concentration.

2. All IC50s have errors of +/ -50%.

Figure 2: Example polymerization curves for MCF-7 cell tubulin (Cat. # H005)



References

Davis A, Martinez S, Nelson D. and Middleton K. 2009. A Tubulin Polymerization Microassay Used to Compare Ligand Efficacy. Meth. Cell Biol. 95, Ch 18, p.327-347.