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Recommendation for the Award of Distinction - PhD Thesis of Anoop Kallingal

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I strongly recommend Anoop Kallingal's PhD thesis, titled 'Mechanistic studies on selected novel anticancer compounds modulating the function of telomeric proteins', for the award of distinction.

My recommendation is based on the identification and biological characterization of promising small-molecule leads for telomere-directed anticancer drug development. A particularly notable achievement is the demonstration that derivatives of the parent compound A822 retain anticancer activity while substantially improving cancer-to-normal-cell selectivity in defined experimental models. TRFiN72 showed median selectivity indices of 5.18 in the breast cancer panel and 2.00 in the colon cancer panel, compared with 0.52 and 0.10, respectively, for A822, while maintaining comparable low-micromolar anticancer activity.

The potential of these compounds is further supported by inhibition of tumor spheroid growth and reduced microtumor weight in an avian chorioallantoic membrane model. Moreover, the combination of direct TRF1-binding measurements with analyses of replication stress and structural telomere abnormalities provides a mechanistic basis for their further investigation. Although additional studies are required to establish intracellular target specificity and a therapeutic window, the dissertation demonstrates experimentally supported improvements over the parental compound and provides a concrete foundation for further optimization of this compound series.

The dissertation is an excellent piece of scientific work, reflecting a substantial research effort, a high level of scientific maturity and the candidate's ability to address complex biological questions.

Overall, I consider this thesis to be of outstanding scientific quality and fully deserving of the award of distinction.

Sincerely,

Claus M. Azzalin 