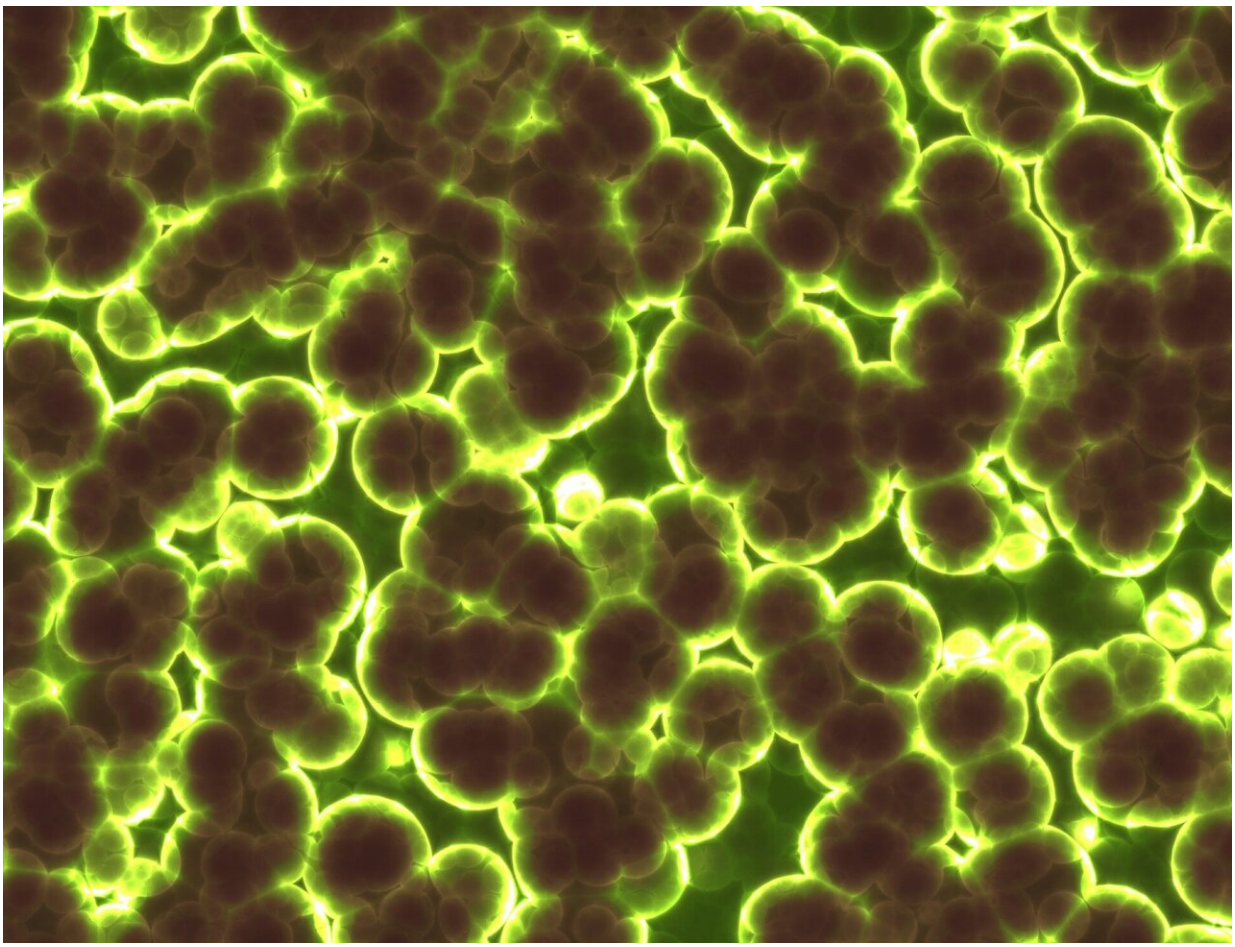
Medical Xpress

How a super-toxic natural product could help develop more effective anti-cancer drugs

June 6 2019



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A new study by a chemistry researcher at the University of Arkansas has

revealed the critical molecular mechanisms of Ipomoeassin F, a highly toxic natural product that inhibits the growth of many tumor cell lines. The finding could lead to the design of more effective anti-cancer drugs.

Ipomoeassin F is a member of the family of resin glycosides, which are secondary metabolites unique to morning glory, a common plant. Ipomoeassin F significantly inhibits growth of many tumor cell lines between 5 to 10 nanometers, which is comparable with many clinical anti-cancer drugs, but until now investigators had not been able to understand its biological and pharmacological mechanisms.

Zhijian Hu, doctoral student in the Department of Chemistry and Biochemistry, tested cytotoxicity of almost 60 analogues—similar chemical compounds—to understand the structural properties of Ipomoeassin F. Hu then used biotin-containing analogues that possessed similar bio-activity to purify and identify Sec61α as the critical protein through the unique binding between biotin and Sec61α. Fluorescent imaging validated the finding.

The fluorescent signal was found to be localized in endoplasmic reticulum, a network of membranes in the cytoplasm of the eukaryotic cell where Sec61α resided. Hu used Western blot, a common method to detect and analyze proteins, to further validate Sec61α as the primary molecular target.

The study, published in the *Journal of the American Chemical Society*, provides a new molecular tool to further understand Sec61α properties and its potential to be a new therapeutic target for drug discovery.

Zhijian Hu

More information: Guanghui Zong et al. Ipomoeassin F Binds Sec61α to Inhibit Protein Translocation, *Journal of the American Chemical Society* (2019). DOI: 10.1021/jacs.8b13506

Provided by University of Arkansas