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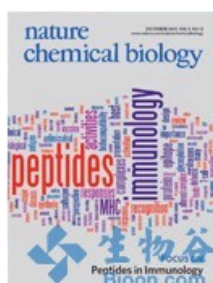
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电影《非诚勿扰II》的热映, 让很多人认识了被称为“癌症王中王”的黑色素瘤。近日, 厦门大学生命科学学院吴昊课题组和林天伟教授课题组合作, 发现了通过诱导细胞自噬性死亡从而有效抑制黑色素瘤细胞生长的信号通路。该研究为治疗黑色素瘤开启新思路, 提供新靶点和独特的先导化合物。相关论文日前在线发表于《自然—化学生物学》。

吴昊课题组研究发现, 当把THPN这一小分子化合物与黑色素瘤细胞孵育后, 一连串“神奇”的反应就开始了: TR3携带到线粒体上, 并通过线粒体外膜蛋白Toms的引导, 跨越线粒体外膜与内膜蛋白ANT1结合, 从而打开线粒体膜“开关”, 使一些内含物流进或流出, 产生线粒体膜电位的下降和ATP能量异常, 引发细胞过度自噬, 最终导致黑色素瘤细胞走向不可逆的自噬性死亡。

林天伟课题组则从原子水平上进一步探明了THPN与TR3结合的构象和精确位点, 为机理研究提供了重要证据。(生物谷推荐) [\(Bioon.com\)](#)

生物谷推荐的英文摘要



Nature Chemical Biology

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Orphan nuclear receptor TR3 acts in autophagic cell death via mitochondrial signaling pathway

Wei-jia Wang, Yuan Wang, Hang-zi Chen, Yong-zhen Xing, Feng-wei Li, Qian Zhang, Bo Zhou, Hong-kui Zhang, Ji Zhang, Xue-li Bian, Li Li, Yuan Liu, Bi-xing Zhao, Yan Chen, Rong Wu, An-zhong Li, Lu-ming Yao, Ping Chen, Y Zhang, Xu-yang Tian, Friedrich Beermann, Mian Wu, Jiahuai Han, Pei-qiang Huang, Tianwei Lin

Autophagy is linked to cell death, yet the associated mechanisms are largely undercharacterized. We discovered that melanoma cells, which is generally resistant to drug-induced apoptosis, can undergo autophagic cell death with the participation of orphan nuclear receptor TR3. A sequence of molecular events leading to cellular demise is launched by a specific chemical compound, 1-(4, 5-trihydroxyphenyl)nonan-1-one, newly acquired from screening a library of TR3-targeting compounds. The autophagic cascade comprises TR3 translocation to mitochondria through interaction with the mitochondrial outer membrane protein Niemann-Pick C2-related protein 1, crossing into the mitochondrial inner membrane through Tom40 and Tom70 channel proteins, dissipation of mitochondrial membrane potential by the permeability transition pore complex ANT1 - VDAC1 and induction of autophagy. This process leads to excessive mitochondria clearance and irreversible cell death. It implicates a new approach to melanoma therapy through activation of a mitochondrial signaling pathway that integrates a nuclear receptor with autophagy for cell death.

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