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AJ-5 inhibits melanoma growth in vitro and in vivo through apoptosis and autophagy

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Recently, palladium based compounds have been investigated as potential anti-tumor agents against several cancers including melanoma. However, very little is known about their mechanism of action and whether they have any side effects in vivo is not known. This study describes the anti-tumor activity of AJ-5, a novel binuclear palladacycle complex in vertical growth phase (ME1402) and metastatic (WM1158) melanoma cell lines in vitro and in vivo. Compared to normal control cell lines, AJ-5 was shown to be more effective in inhibiting the proliferation of melanoma cells with IC50 values of less than or equal to 0.20 μ M. Flow cytometry analyses showed that AJ-5 induced apoptosis which was confirmed by Annexin V-FITC/propidium iodide double-staining, nuclear fragmentation and an increase in the levels of PARP cleavage. Furthermore, AJ-5 was shown to induce both intrinsic and extrinsic apoptotic pathways as measured by PUMA, Bax, cytochrome c release and active caspases. Interestingly, AJ-5 treatment also simultaneously induced the formation of autophagosomes and led to an increase in the autophagy markers LC3II and Beclin1. Inhibition of autophagy reduced AJ-5 cytotoxicity suggesting that AJ-5 induced autophagy was a cell death and not cell survival mechanism. Moreover, it was shown that AJ-5 induces the ATM-CHK2 DNA damage pathway and that its anti-tumor function is mediated by the p38 and ERK1/2 signaling pathways. Importantly, AJ-5 treatment efficiently reduced tumor growth in melanoma bearing mice and induced high levels of autophagy and apoptosis markers.

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Anal canal melanoma misdiagnosed and treated as prolapsed hemorrhoids in a male patient

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Malignant melanoma of the anal canal is a rare but aggressive tumor with a poor prognosis. It represents less than 1% of all melanomas and 4% of anorectal tumors. We are reporting this case because of its rarity in men and because, in this instance, the tumor was misdiagnosed as prolapsed thrombosed hemorrhoids and excised. Examination showed a visible exophytic irreducible growth measuring about 3×3 cm and protruding outside the anal verge and involving the anterior two-thirds of the circumference of the anal canal. A biopsy sample showed round to oval cells with prominent nucleoli and marked intracytoplasmic pigmentation. A magnetic resonance imaging scan showed a tumor with nearly complete luminal obstruction and liver metastasis. The patient received chemotherapy and radiotherapy, but the response was very poor and he died 2 months later.

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