

# Synergistic activity for pevonedistat with BRAF kinase inhibitors in BRAF melanoma

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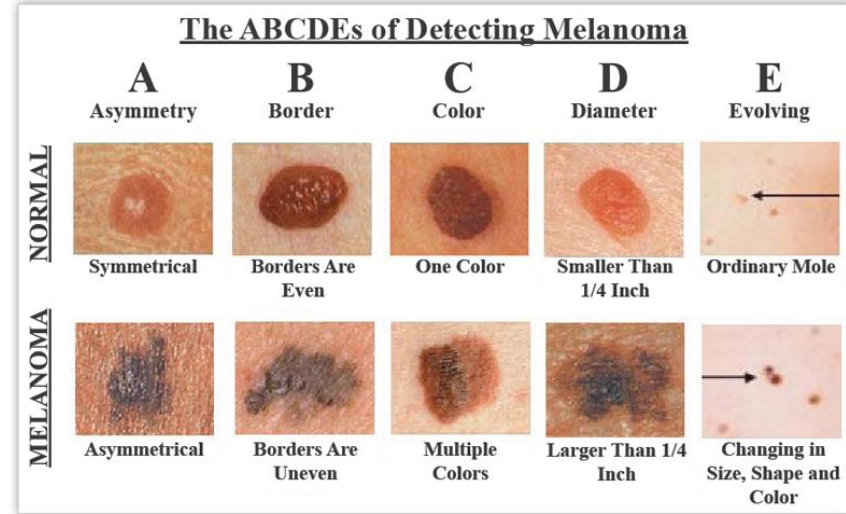
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# Melanoma

- The most dangerous form of skin cancer, these cancerous growths develop when unrepaired DNA damage to skin cells triggers mutations that lead the skin cells to multiply rapidly and form malignant tumors
- Activating mutations in the serine/threonine kinases BRAF or NRAS occur in a majority of cases
- Clinical Problem:
  - Affects ~80,000 patients/year in the U.S.
  - Current treatments with BRAF inhibitors are only effective for a subset of melanoma patients

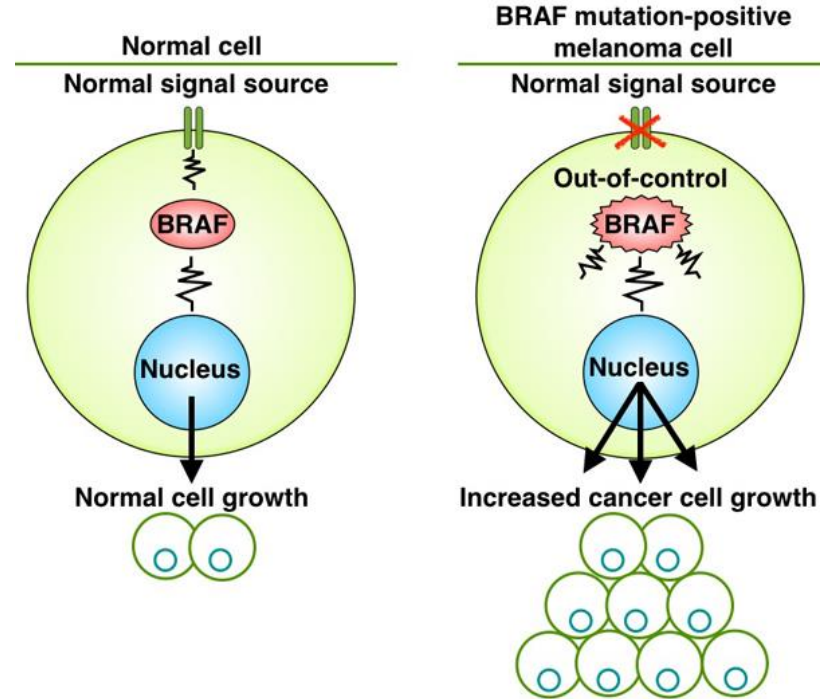


Dyersburg Skin and Allergy Clinic

# Combination therapy for melanoma

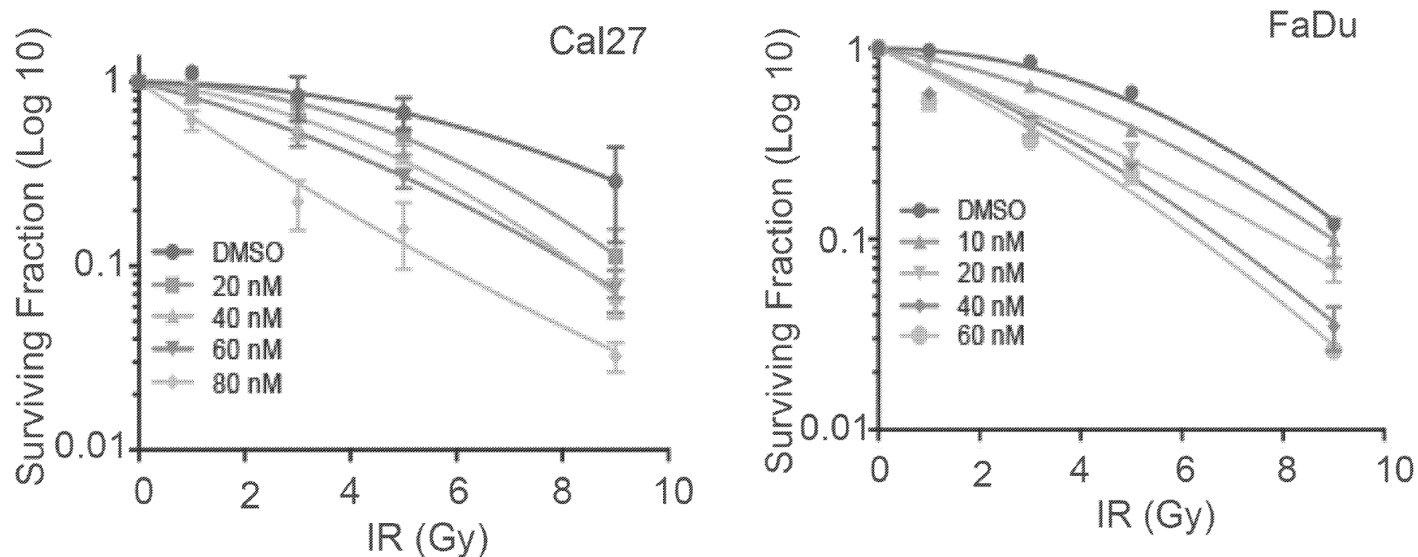
**Solution:** Researchers at the University of Virginia have determined that the combination of pevonedistat and BRAF kinase inhibitors work synergistically in the treatment of melanoma

- BRAF kinase inhibitors combined with pevonedistat yields synergistic suppression in BRAF mutant melanoma
- Potential use for treatment of melanoma, as well as head and neck cancers



# Pevonedistat dose-dependently increased radiosensitivity *in vivo*

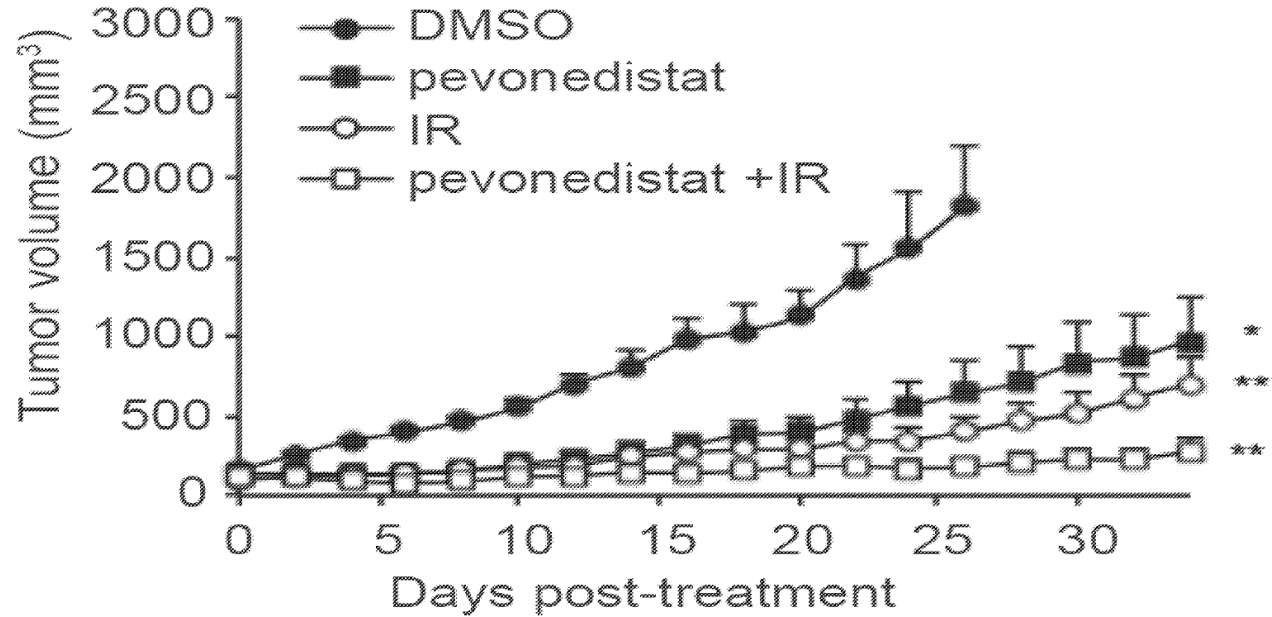
## Head and neck squamous cell carcinoma (HNSCC) cell lines



Pevonedistat was administered 24 hrs. prior to irradiation with indicated doses. Surviving fractions were determined by dividing the number of colonies present in cells treated by the number of colonies from a non-irradiated control cell group.

# Pevonedistat suppressed HNSCC xenograft growth

Pevonedistat, irradiation alone (IR) or pevonedistat + IR was administered to HNSCC tumors and tumor volume was measured up to 30 days post-treatment.



# Relevant Publications

- EBioMedicine. 2016 Aug;10:85-100. **Abbas T**, et. al.

# Intellectual Property

- UVA Tech ID: ABBAS-COMBINATION
  - Title: Compositions and methods for treating cancer
  - PCT Application PCT/US2017/029859 filed Apr. 27, 2017