

# Newcastle Melanoma Unit

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## Current Clinical Trials

Co-Investigator – Randomized Trial of Sentinel Node Biopsy in Stage II, III Melanoma.

MSLT-11 Commenced 8/2005. Ongoing.

Principal Investigator – A Phase I Study of Intralesional PV-10 Chemoablation in Subjects with Metastatic Melanoma. Commenced 9/2005.

Co-Investigator - Phase 2 Clinical Trial of 17-allylamino-17-demethoxy-geldanamycin (KOS-953) in Metastatic Melanoma. Sponsor: Kosan Biosciences. Commenced May 2006.

Co-Investigator – Phase 2, Open Label, Single Arm Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of CP-675,206 in Patients with Advanced Refractory and/or Relapsed Melanoma (A3671008). Sponsor: Pfizer. Commenced May 2006.

Co-Investigator – A Phase 3, Open Label, Randomized, Comparative Study of Ticitimumab and Either Dacarbazine or Temozolomide in Patients with Advanced Melanoma (A3671009). Sponsor: Pfizer. Commenced May 2006.

Co-Investigator – A Phase II, Multi-centre, Open-Label, Parallel Group, Randomised Study to Assess the Safety and Efficacy of AZD6244 vs Temozolomide in Subjects with Unresectable AJCC Stage 3 or 4 Malignant Melanoma. Sponsor: AstraZeneca. Commenced June 2006.

Co-Investigator – A Phase III Randomized, Double Blind, Multinational, Multicenter Study of Study Therapy in Combination with Dacarbazine in Treating Patients with Unresectable, Stage IV or Recurrent Stage III Melanoma (CA184-024). Sponsor: Medarex/Bristol Myer Squibb. (To be commenced)

Co-Investigator – A Randomized, Double-Blind, Multi-center, Phase II Fixed Dose Study of Multiple Doses of BMS-734016 (MDXI-010) Monotherapy in Patients with Previously Treated Unresectable Stage III or IV Melanoma (CA184-022). Sponsor: Medarex/Bristol Myer Squibb. (To be commenced)

## Recent Publications

Hersey, P., Menzies, S.W., Coventry, B., Nguyen, T., Farrelly, M., Collins, S., Hirst, D., and Johnson, H. (2005) Phase I/II study of immunotherapy with T cell peptide epitopes in patients with stage IV melanoma. *Cancer Immunology Immunotherapy* 54(3): 208-218. (IF: 3.130)

Gillespie, S.K., Zhang, X.D. and Hersey, P. (2004) Ingenol 3-angelate induces dual modes of cell death and differentially regulates TRAIL-induced apoptosis in melanoma cells. *Molecular Cancer Therapeutics* 3:1651-1658. (IF: 3.201) Bron, L.P., Scolyer, R.A.,

Thompson, J.F. and Hersey, P. (2004) Histological expression of tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) in human primary melanoma. *Pathology* 36(6):561-565. (IF: 1.112)

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- Gillespie, S., Zhang, X.D. and Hersey, P. (2005) Variable expression of protein kinase C epsilon in human melanoma cells regulates sensitivity to TRAIL-induced apoptosis. *Molecular Cancer Therapeutics* 4(4):668-76. (IF: 3.201)
- Byrne, C.M., Thompson, J.F., Johnston, H., Hersey, P., Quinn, M.J., Hughes, T.M. and McCarthy, W.H. (2005) Treatment of metastatic melanoma using electroporation therapy with bleomycin (electrochemotherapy). *Melanoma Research* 15:45-51.
- Allen, J.D., Zhang, X.D., Scott, C.L., Boyle, G.M., Hersey, P. and Strasser, A. (2005) Is Apaf-1 expression frequently abrogated in melanoma? (Letter) *Cell Death & Differentiation* 12(6):680-1.
- Wu, J.J., Zhang, X.D., Gillespie, S. and Hersey, P. (2005) Selection for TRAIL resistance results in melanoma cells with high proliferative potential. *FEBS Letters* 579(9):1940-1944.
- Zhuang, L., Lee, C.S., Scolyer, R.A., McCarthy, S.W., Palmer, A.A., Zhang X.D., Thompson, J.F., Bron, L.P. and Hersey, P. (2005) Activation of the extracellular-signal related kinase (ERK) pathway in human melanoma. *J. Clin. Pathology* 58(11):1163-1169. IF: 2.966
- Millward, M.J., Joshua, A., Kefford, R., Aamdal, S., Thomson, D., Hersey, P., Toner, G. and Lynch, K. (2005) Multi-centre Phase II trial of the polyamine synthesis inhibitor SAM486A (CGP48664) in patients with metastatic melanoma. *Invest. New Drugs* 23(3):253-6.
- Zhang, X.D., Wu, J.J., Gillespie, S.K., Borrow, J.M., and Hersey, P. (2006) Human melanoma cells selected for resistance to apoptosis by prolonged exposure to TRAIL are more vulnerable to necrotic cell death induced by Cisplatin. *Clin. Cancer Res.* 12(4):1355-1364. IF: 6.511
- Hersey, P. Apoptosis and melanoma: how new insights are effecting the development of new therapies for melanoma. (2006) *Current Opinion in Oncology* 18:189-196. IF: 4.544
- Hersey, P., Zhuang, L., and Zhang, X.D. Current strategies in overcoming resistance of cancer cells to apoptosis melanoma as a model. (2006) *International Review of Cytology* 251:131-158.
- Zhuang, L., Lee, C.S., Scolyer, R.A., McCarthy, S.W., Zhang, X.D., Thompson, J.F., Screatton, G., and Hersey, P. (2006) Progression in melanoma is associated with decreased expression of death receptors for tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). *Human Pathology* 37:1286-1294.
- Bedikian, A., Millward, M., Pehamberger, H., Conry, R., Gore, M., Sterry, W., Pavlick, A.C., DeConti, R., Hersh, E.M., Hersey, P., Kirkwood, J.M., Haluska, F.G., the Oblimersen Melanoma Study Group. (2006) Bcl-2 antisense (Oblimersen Sodium) plus Dacarbazine in patients with advanced melanoma. *J. Clin. Oncol.* 24:4738-4745.
- Yu, F., Watts, R., Zhang, X.D., Borrow, J.M., and Hersey, P. (2006) Involvement of BH3 only proapoptotic proteins in mitochondrial dependent Phenoxodiol induced apoptosis of human melanoma cells. *Anticancer Drugs* 17(10):1151-1161.
- Gillespie, S., Borrow, J., Zhang, X.D., and Hersey, P. (2006) Bim plays a crucial role in synergistic induction of apoptosis by the histone deacetylase inhibitor SBHA and TRAIL in melanoma cells. *Apoptosis* 11(12):2251-2265.
- Zhang, X.D., Wu, J.J., Gillespie, S., Borrow, J., and Hersey, P. (2006) Cross resistance of melanoma to trail-induced apoptosis and chemotherapy. *Update on Cancer Therapeutics* (in press).
- Mhaidat, N.M., Wang, Y., Kiejda, K., Zhang, X.D., and Hersey, P. (2006) Docetaxel induced apoptosis in melanoma is dependent on activation of Caspase 2. *Mol. Canc. Therapeutics* (in press).
- Mhaidat, N.M., Zhang, X.D., Jiang, C.C., and Hersey, P. (2006) Docetaxel-induced apoptosis of human melanoma is mediated by activation of JNK and inhibited by the MAPKinase ERK1/2 pathway. *Clinical Cancer Research* (Accepted for publication).
- Zhuang, L., Lee, C.S., Scolyer, R.A., McCarthy, S.W., Zhang, X.D., Thompson, J.F., and Hersey, P. (2006) Mcl-1, Bcl-XL and Stat3 expression are associated with progression of melanoma whereas Bcl-2, AP-2 and MITF levels decrease during progression of melanoma. *Modern Pathology* (in press).

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### Book Chapters

Zhang, X.D., Wu, J.J., Gillespie, S., Borrow, J. and Hersey, P. (2005) Cross resistance of melanoma to TRAIL induced apoptosis and chemotherapy. In: Cancer Chemotherapy & Biological Response Modifiers Annual.

Hersey, P. (2005) Immunotherapy of Melanoma – Past, Present and Future. In: Cancer Forum. The Cancer Council, Australia.

Hersey, P., Zhuang, L. and Zhang, X.D. (2006). Current strategies in overcoming resistance of cancer cells to apoptosis. Melanoma as a model. In: International Review of Cytology – A Survey of Cell Biology. Ed: Jeon, K.W. Elsevier, California. P131-158.

Hersey, P. (2006). Apoptosis and Melanoma. How new insights are effecting the development of new therapies for melanoma. In: Current Opinion in Oncology (in press).

Hersey, P., Zhang, X.D. and Mhaidat, N. (2006). Overcoming resistance to apoptosis in cancer therapy. In: Programmed Cell Death in Cancer Progression and Therapy. Eds: Khosravi-Far, R. and White, E. (in press).