

The following are abstracts of three papers presented orally at the 3rd Annual Moffitt Fellow Research Symposium at the H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, on May 11, 2009.

PKC theta targeting inhibits alloreactivity and GVHD while preserving the GVL effect

Iclozan C, Valenzuela JO, Hopewell E, Hossain MS, Waller EK, Yu X-Z, and Beg AA

Objectives: (1) Recognize PKC theta isotype as a crucial drug target that has clinical potential to alleviate or prevent graft-vs-host disease (GVHD) while sparing graft-vs-leukemia (GVL) and antiviral activity. (2) Learn that future therapeutic options in allogeneic bone marrow transplantation (BMT) or organ transplantation could include the use of selective inhibitors of PKC theta. **Introduction:** Protein kinase C theta isoform (PKC θ) is crucial in T-cell-receptor signaling and regulates the nature of lymphocyte-specific in vivo effector responses. The aim of this study was to investigate the significance of PKC θ in donor T-cell-mediated GVHD, antileukemia, and antiviral infection. **Methods:** Our results were validated using clinically relevant murine BMT system. GVHD was measured by recipient survival and clinical signs such as body weight loss. Leukemia was induced by intravenous injection of a luciferase-expressing A20 clone (a B lymphoma cell line derived from BALB/c mice). Further, tumor invasion was quantitated using the Xenogen IVIS-200 bioluminescence imaging system. Murine cytomegalovirus (MCMV) infection was induced by intraperitoneally injecting 2×10^4 PFU/mouse in the recipients after GVHD was established. **Results:** Allogeneic BMT as cancer immunotherapy frequently leads to GVHD, functional immunodeficiency and an increased risk of infections. Our experiments show that PKC θ knock-out (KO) T cells do not induce GVHD while preserving the GVL effect. In murine allogeneic BMT models, we found that recipients of PKC θ KO T cells had significantly less GVHD morbidity and mortality compared with recipients of wild-type (WT) donor T cells. Using A20-luciferase+ cell line, we observed the absence of tumor growth in mice transplanted with PKC θ KO T cells. When analyzing viral loads in spleens and livers from mice with chronic GVHD (after receiving nonlethal doses of MCMV), PKC θ KO T cells appear to fight the MCMV infection similar as the WT ones. These data were confirmed by immunostaining with MCMV peptide-specific tetramer on CD8+ T cells from spleen. We identify herein that PKC θ KO T cells used in allogeneic BMT are unable to induce GVHD while preserving donor T-cell-mediated GVL and anti-infection activities. **Conclusions:** Our

work provides strong rationale to use selective inhibitors of PKC θ as novel therapeutic options in allogeneic BMT or organ transplantation.

Use of sentinel node biopsy in DCIS: when do you find a positive node?

McGuire KP, Lee MC, Kiluk J, Khabkpour N, and Laronga C

Objectives: Identify the rate of positive sentinel lymph node after surgery for DCIS and identify the clinicopathologic factor(s) associated with sentinel lymph node positivity after surgery for DCIS. **Introduction:** Performing sentinel lymph node biopsy (SLNB) on patients with ductal carcinoma in situ (DCIS) remains controversial, especially if the diagnosis is made on core needle biopsy (CNB). Our objective was to assess the features associated with SLN-positive disease in patients with DCIS on core biopsy to improve the preoperative selection process. **Methods:** A prospective database of surgically treated breast cancer patients was reviewed for patients with a sole diagnosis of DCIS on CNB (1997–2008). The patients' age, race, personal and family history of breast cancer, tumor biology, type of surgery, SLNB results, and follow-up data were recorded. **Results:** A total of 407 patients with DCIS on CNB underwent surgical therapy involving SLNB. Of 407 patients, 291 (71%) had a final diagnosis of DCIS. The remaining 116 patients (29%) had invasive cancer. Median age was 56 (25–90), median follow-up was 39 months (1–136), 236 (58%) had a lumpectomy, and 171 (42%) had a mastectomy. The median number of sentinel nodes was 2 (0–6). Of the 407 patients, 31 (7.6%) had a positive SLNB at the time of surgery. Of 291 patients, 11 (3.8%) with a final diagnosis of DCIS had positive SLN vs 20 of 116 (17%) patients upstaged to invasive carcinoma postoperatively ($P = .0001$). Of the 31 patients with a positive SLN, 27 (87%) exhibited comedonecrosis (CN) vs 178 (47%) of 376 patients with negative SLN ($P = .0016$). Of the 27 with CN, 9 (33%) showed DCIS only on final pathology and 18 (67%) showed invasive carcinoma. There were no significant differences in age, race, tumor grade, or receptor status (ER/PR) relative to SLN status. Local recurrence was seen in 10% of patients, regardless of SLN status. **Conclusions:** Our study confirms that the rate of positive SLN at surgery for suspected DCIS is < 10%. If only DCIS is found on final pathology, the positive SLN rate is even lower. In our series, the only preoperative factor

predictive of SLN positivity was the presence of comedonecrosis. This study supports the conclusion of others that SLNB may not change the outcome in DCIS-only patients, but those with comedonecrosis may benefit from the prognostic information gained from SLNB.

Fatigue after treatment for early-stage breast cancer: a controlled comparison

Faul LA, Asvat Y, and Jacobsen PB

Objectives: (1) Demonstrate a greater understanding of differential rates of fatigue among breast cancer survivors compared with healthy controls matched on age, gender, and geographic location, (2) explicate methodological weaknesses in previous studies examining fatigue among cancer survivors, and (3) identify potential implications of the present findings on the design and implementation of interventions targeting the reduction of fatigue among cancer patients and survivors. **Introduction:** Fatigue is among the most common problems reported by cancer survivors. However, it is unclear to what extent fatigue is a greater problem for cancer survivors than for people without cancer. Previous results, largely inconsistent, have been confined by differences in measurement and methodology. The current study sought to address this question via utilization of matched controls and a homogenous cancer survivorship population. **Hypothesis:** We predicted that breast cancer patients would report greater fatigue at the end of treatment but that there would be a decrease to levels comparable to the control group at 12 months posttreatment. **Methods:** We compared 122 patients treated for early-stage breast cancer to 122 controls matched for age, gender, and geographical location. Using the Fatigue Symptom Inventory (FSI) and the Profile of Mood States Fatigue Scale (POMS-F), data were gathered at the end of active treatment and at 12 months posttreatment. **Results:** As expected, patients experienced significantly greater levels of overall and current fatigue, average fatigue, fatigue severity, total days fatigued, and disruptiveness caused by fatigue ($P < .05$) than controls at the end of treatment. However, by 12 months posttreatment, patients displayed significant differences relative to controls only on current fatigue ($P = .03$) and number of days fatigued ($P = .01$). Breast cancer patients experienced significant recovery over time on levels of fatigue severity, average fatigue, current fatigue, and total days fatigued ($P < .01$). **Conclusions:** Overall, breast cancer patients experience more fatigue at the end of treatment than the general population, with fatigue symptoms diminishing over time. Development of interventions targeting fatigue would be especially useful immediately following treatment. Utilizing matched controls and homogeneous patient groups, this phenomenon merits additional investigation across other cancer types as the effects of cancer and its treatment vary widely.

The following three papers also were presented orally at the 3rd Annual Moffitt Fellow Research Symposium at the H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, on May 11, 2009. The abstracts have been published elsewhere.

BETA1 integrin adhesion enhances IL-6-mediated STAT3 signaling in myeloma cells: implications for microenvironment influence on tumor survival and proliferation

Shain KH, Yarde DN, Meads MB, Huang M, Jove R, Hazlehurst LA, and Dalton WS

Cancer Res. 2009;69(3):1009-1015. Epub 2009 Jan 20. <http://cancerres.aacrjournals.org/cgi/content/abstract/69/3/1009>

Predictive scoring systems for brain metastasis at diagnosis and recurrence in non-small cell lung cancer

Maunglay ST, Fulp WJ, Chiappori A, and Simon GR

2009 ASCO Annual Meeting Abstracts. *J Clin Oncol.* 2009;(suppl):e19020. http://www.abstract.asco.org/AbsView_65_33696.html

Molecular predictors of response to neoadjuvant topotecan and radiation for rectal cancer: correlative study to a phase I trial

Santillan AA, Dinwoodie WR, Yeatman TJ, Eschrich SA, Sullivan D, Rocha Lima CM, Greenberg HM, Chodkiewicz C, Trotti A, Marcet JE, Dessureault S, Legenne P, Wissel P, Tyagi P, and Shibata D

The Society for Surgery of the Alimentary Tract. <http://www.ssat.com/cgi-bin/abstracts/09ddw/QS13.cgi>