Identification of New Therapeutic Drugs for Triple-Negative Breast Cancer

Paul Mintz

Judy A. Tjoe

Follow this and additional works at: https://aurora.org/jpcrr

Part of the Medical Genetics Commons, Neoplasms Commons, Oncology Commons, Therapeutics Commons, and the Translational Medical Research Commons

Recommended Citation
Background: Delirium is an acute change in mental status commonly seen in hospitalized older adults. Although the occurrence of delirium is serious and is associated with adverse outcomes, patients with delirium may be prescribed antipsychotics/benzodiazepines, which may lead to potential side effects and other complications. The Hospital Elder Life Program (HELP) is a national evidence-based program designed to prevent delirium and functional decline. Research demonstrates that HELP decreases the onset and/or length of delirium episodes, functional decline in hospitalized older adults, and readmission rates, promotes nonpharmacological interventions, and is a cost-effective method for improving outcomes.

Purpose: To evaluate 30-day readmission percentage and assess the prevalence of newly prescribed antipsychotic/benzodiazepine medication prior to discharge among HELP-enrolled patients at a large medical center.

Methods: We conducted a retrospective study of patients ≥ 65 years of age who were admitted and enrolled into 1 of the 8 HELP units in 2016 or 2017. Patient characteristics were described using basic descriptive statistics. Odds ratios were calculated as the odds of having antipsychotics/benzodiazepines prescribed at admission versus those who were not. Chi-squared tests were performed to detect statistical differences among nominal variables. A P-value less than 0.05 was deemed significant.

Results: 1400 patients (mean age: 80; range: 65–100) were enrolled into HELP. Overall, 25% (n=355) of patients were recorded to have been readmitted within 30 days of initial discharge from a HELP unit. This number was not significantly associated with antipsychotic/benzodiazepine prescription at admission (P=0.8575). Yet, when examining sex differences, females patients were more likely to receive a new antipsychotic/benzodiazepine prescription at admission (P<0.0001). Similarly, having a mental illness diagnosis at the time of admission made one more likely to have antipsychotics/benzodiazepines prescribed (P<0.0001).

Conclusion: One-quarter of patients in HELP were readmitted within 30 days of discharge. Moreover, patients enrolled in HELP with a mental illness diagnosis prior to admission were more likely to receive antipsychotic/benzodiazepine prescription at admission. Further studies could assist defining steps to decrease high-risk medications prescribed to HELP-enrolled patients with a history of mental illness.

Identifying New Therapeutic Drugs for Triple-Negative Breast Cancer

Paul Mintz, Judy A. Tjoe

TORQUE, Aurora Research Institute; Surgical Oncology, Aurora Cancer Care

Background: The development of cancer is a multistep process of sequential genetic alterations in oncogenes and tumor-suppressor genes, making it extremely challenging to find a cure for cancer. In the case of breast cancer, patients diagnosed with triple-negative breast cancer (15%–20%) have the worst survival outcome and no new treatment options. It is characterized by having no or low expression level of three genes, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor type 2 (HER2), which makes it more difficult to develop therapeutic agents. A new targeting approach is greatly needed to identify novel drug targets for triple-negative breast cancer.

Purpose: We have taken a drug-targeting approach to identify new drug targets for triple-negative breast cancer. We propose to test Food and Drug Administration (FDA)-approved drugs on patient-derived triple-negative breast cancer primary cells generated from patient tissue.

Methods: Residual tissue samples from triple-negative breast cancer surgery were processed and the dissociated cells were grown in a specific tissue-culture medium containing supplements. A triple-negative primary cell line was authenticated by an independent company to demonstrate that it was a true cell line (DNA fingerprinting). A panel of FDA-approved drugs was tested on the primary cell line to identify new therapeutic drugs.
Molecular and cellular assays, including cell proliferation and cytotoxicity, were used to determine the effect of the drugs on the cells. Specific cell signaling pathways were investigated to discover the mechanism of action.

**Results:** We have successfully established a triple-negative breast cancer patient-derived primary cell line, the first at Aurora Health Care. The triple-negative cells are negative for the three known receptors (ER, PR, HER2) but positive for cytokeratin 5 and 8/18 by immunocytochemical staining. We have identified several potential FDA-approved drugs that inhibit triple-negative cells from growing. Selected drugs are being further investigated for their mechanism of action.

**Conclusion:** To address the limited treatment options for patients diagnosed with triple-negative breast cancer, we have taken a drug-targeting strategy. Repurposing FDA-approved drugs for triple-negative breast cancer could be a powerful approach to discovering new therapeutics to improve patient care.

**‘Difficult Teaching Case’ Conference Call Series — A Faculty Development Strategy**


*Departments of Family Medicine, Academic Affairs, Population Health, and Obstetrics and Gynecology, Aurora UW Medical Group; Department of Medicine, Aurora BayCare Medical Center*

**Background:** Teaching requires a unique knowledge and skill set, from competency-based assessment to digital fluency and teaching of interprofessional teams. However, barriers to faculty development such as lack of time to prepare, incentives, and isolation/lack of support for one’s identity as a clinician teacher are well enumerated, as are the elements of successful programs.

**Purpose:** To implement an ongoing faculty development case conference call series that expands participants’ teaching strategies, increases their confidence as educators, and strengthens their connections to other teachers.

**Methods:** Case discussion is signature pedagogy in medical education as it makes the reasoning underlying one’s decisions as a clinician or teacher visible and promotes deeper learning. Using a teaching-focused case methodology, we implemented a monthly 45-minute teaching case conference call series. Participants receive a one-screen email precis of the case 1–2 days in advance and then dial into a conference call. The case is sequentially reviewed with conference participants asking questions/explaining how they may frame the “assessment” and “plan.” The conference ends with key teaching pearls/take-home points, with follow-up readings/resources distributed postconference and a brief evaluation.

**Results:** Cases have ranged from clinical teaching (a learner who “never got feedback”) and small-group teaching (a learner who was offended by a teacher’s analogy), to unprofessionalism (disruptive/argumentative learners), to teaching the “rock star” residents. Average number of participants was 7, with an upper limit of 11; 18 different physicians and 8 different nurse practitioners have attended at least 1 of the 10 sessions. Evaluations reveal that all participants agree that the case scenario was relevant/important, expanded teaching strategies, and connected them to others who value teaching. Typical comments include “these sessions are extremely valuable and will improve our learning culture...” and “it’s a relief that I’m not the only one to have had this happen....

**Conclusion:** Clinical teachers highly value the difficult teaching case conference call series. The approach is easily transferable to other organizations, requiring no advance participant preparation, and uses telephone access to offer a “safe” place to explore and learn from colleagues’ difficult teaching situations and affirm their roles and value as teachers.

**Evaluating Well-Being in OB/GYN Residents and Faculty**

Erika Copperman, Naomi Light, Carla J. Kelly, Deborah Simpson

*Department of Obstetrics and Gynecology, Aurora Sinai Medical Center; Departments of Obstetrics and Gynecology, Family Medicine, and Academic Affairs, Aurora UW Medical Group*

**Background:** Between 22% and 60% of practicing physicians are reported to have experienced burnout. OB/GYN resident burnout has been reported at 90%. Duty-hour limitations were implemented for patient safety and have been associated with some increase in overall resident quality of life, but also potential sacrifices in resident education and patient care. Contributors to burnout and drivers of engagement include workload and job demands, control and flexibility, and poor work-life integration.

**Purpose:** To evaluate the impact associated with implementing limited weekend rounding, redistribution of postpartum rounding on weekdays, and introduction of quarterly wellness mornings on overall resident and faculty well-being.

**Methods:** Effective July 2, 2017, two workload protocols were changed. Weekend rounding protocols continue to have residents round on all antepartum and gynecology patients at the end of each 24-hour shift, but now faculty complete all postpartum rounding. Weekday postpartum rounding was redistributed, decreasing the number of patients per junior resident from > 10 patients to a maximum of 6–7 patients per resident. Quarterly wellness mornings began in September 2017, using protected education time for faculty and resident physicians. A brief 3-item well-being check-in card (WBCIC) was developed and used to obtain participants’ quarterly ratings regarding the adequacy of time for wellness, level of meaning in their work, and comments. Debriefings during resident-required curriculum time provided perspective on impact of reduced rounding protocols.

**Results:** Mean WBCIC scores revealed time spent on personal well-being at baseline and 7 months postimplementation was 1.6 and 2.1 for residents, respectively, and 2.4 and 2.4 for faculty (Scale: 1=pitiful to 4=excellent). The item “Work I do is meaningful to me” scored 4.9 and 4.1 for residents pre- and postintervention and 5.5 and 6.3 for faculty (Scale: 1=strongly disagree to 7=strongly agree).

**Conclusion:** After changes in rounding, residents’ personal well-being improved but meaning in work declined. In contrast, faculty’s personal well-being remained constant and meaning in work increased. Additional well-being interventions focused on residents’ meaning in work will be explored.