that the radiocomplex remained intact for up to 24 hours without metal dissociation, indicating its suitability for future in vivo assessments. These promising results pave the way for structural optimization through spacer units and subsequent bioconjugation studies for the development of new radiopharmaceuticals.

Keywords: Gallium, Radioisotopes, Theranostics, Hexadentate Chelators, Imine group.

Conflicts of interest: Not declared.

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ROBUST AND RIGOROUS IC50 DETERMINATION FOR PRECLINICAL DRUG DISCOVERY

Letícia Fernanda Alves,
Gilberto Carlos Franchi Júnior,
Alessandra Rodrigues Cardoso Padovam,
Leticia Pires de Oliveira, Pedro Paulo Corbi,
Carmen Silvia Passos Lima,
Diego Samuel Rodrigues

Universidade Estadual de Campinas, Campinas, SP, Brazil

Determining dose-response curves is a critical first step in preclinical drug discovery. Typically, experimental dose-response data are fitted using nonlinear sigmoidal models. This process requires careful attention to fitting criteria and model comparison. Not infrequently, drug candidate compounds may lack sufficient potency at the tested concentrations or produce data that lead to unavoidable poor fitting. A key parameter to estimate in such cases is the half-maximal inhibitory concentration (IC50). This study illustrates the use of the R package drda as the state-of-the-art statistical tool to address these fitting challenges, with a reputation for having been extensively tested in fitting applications with synthetic data and under random sampling from a real dataset of 379,533 cell line and drug pairs. For model evaluation, drda provides the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Likelihood Ratio Test (LRT) to assess goodness of fit for logistic regressions with varying parameter complexities. Combined with graphical diagnostics, results from our benchmark real dataset show that AIC, BIC, and LRT are essential for the rigorous estimation of IC50. In fact, the systematic use of metrics increases reliability in dose-response studies by minimizing the risk of pursuing ineffective compounds and reducing the chance of discarding potentially active molecules, thereby supporting more efficient and innovative preclinical drug discovery.

Keywords: Dose-response data analysis, Model calibration and selection, Preclinical drug discovery.

Conflicts of interest: Not declared.

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EGFR-TARGETING GE11-DERIVED PEPTIDE DIFFERENTIALLY MODULATES TRIPLE-NEGATIVE BREAST CANCER AND GLIOBLASTOMA CELL PROLIFERATION IN VITRO

Julia Naomi Ono, Danielle Vieira Sobral,
Fernanda Ferreira Mendonça,
Luciana Malavolta, Leonardo Lima Fuscaldi

Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil

Introduction: Triple-negative breast cancer (TNBC) represents one of the most aggressive subtypes of breast cancer. Glioblastoma (GBM) is the most lethal primary brain tumor, characterized by poor prognosis. Both malignancies frequently overexpress the epidermal growth factor receptor (EGFR), which contributes to tumor progression by promoting proliferation, angiogenesis, and resistance to apoptosis. The GE11 peptide, YHWYGYTPQNVI, exhibits high affinity for EGFR and has been explored as a targeting ligand in molecular imaging strategies. Here, a modified GE11-derived peptide, YHAYGYTPQNVI, was employed, in which tryptophan was substituted by alanine to reduce photosensitivity. **Objectives:** To evaluate the in vitro effects of the YHAYGYTPQNVI peptide on cell proliferation and viability in TNBC (MDA-MB-231) and GBM (U-87 MG) cells. **Materials and Methods:** MDA-MB-231 and U-87 MG cells were cultured in RPMI-1640 or DMEM, respectively, supplemented with 10% fetal bovine serum (37° C; 5% CO2). Cell proliferation was assessed by growth curve analysis. Cells were seeded in 6-well plates (5×104 cells/well) and treated with YHAYGYTPQNVI (56.1 μM). Viable cell counts were performed on days 1, 3, 5, and 7, comparing with untreated control (CT). Cell viability was evaluated by the MTT assay in MDA-MB-231 cells seeded in 96-well plates (5×10^3 cells/well) and treated with YHAYGYTPQNVI (5.61 μM). MTT measurements were obtained on days 1, 5, and 7, and viability was expressed as a percentage relative to CT. Data are presented as mean $\pm$ SD. Statistical analyses were performed using Student’s *t*-test or ANOVA followed by Tukey’s test, with significance set at $p<0.05$. **Results:** Growth curve analysis of MDA-MB-231 cells revealed no statistically significant differences between the GE11-derived peptide-treated and CT groups, as illustrated on day 7: YHAYGYTPQNVI = $(3.18 \pm 0.40) \times 105$ versus CT = $(3.43 \pm 0.58) \times 105$ [$p = 0.4501$; $n = 6$]. Consistently, MTT assays indicated a moderate reduction in cell viability (~15–25%); however, this reduction was not statistically significant over time, with viabilities of 83.66 $\pm$ 6.24% (day 1), 74.11 $\pm$ 12.24% (day 5), and 79.76 $\pm$ 8.02% (day 7) [$p = 0.1885$; $n = 7$]. In contrast, growth

curve analysis of U-87 MG cells demonstrated a significant inhibition of cell proliferation following treatment with the anti-EGFR peptide. On day 5, treated cells reached (0.87 ± 0.11) × 105 cells compared with (1.67 ± 0.21) × 105 in the CT group [p = 0.0001; n = 6]. This inhibitory effect persisted on day 7, with counts of (1.83 ± 0.23) × 105 versus (3.20 ± 0.66) × 105 for treated and CT cells, respectively [p = 0.0019; n = 6]. MTT assays for the U-87 MG cell line are currently ongoing. The differential responses observed between MDA-MB-231 and U-87 MG cells suggest that EGFR expression alone does not fully predict sensitivity to GE11-derived peptides, indicating the influence of tumor-specific receptor dynamics and downstream signaling mechanisms. **Conclusion:** The YHAYGYTPQNVI peptide exhibited a significant antiproliferative effect in the U-87 MG cells, whereas no comparable response was observed in MDA-MB-231 cells. These findings highlight the heterogeneity of EGFR-mediated interactions across tumor types and support further investigations to elucidate the underlying biological mechanisms. Additional radiolabeling studies may help clarify the potential of this peptide as a targeting molecular imaging probe in EGFR-expressing tumors.

Keywords: Epidermal growth factor receptor, Glioblastoma, Triple-negative breast cancer, Peptides, Cell proliferation.

Conflicts of interest: Not declared.

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EFFECT OF XPC C.2815A>C VARIANT ON CELL CYCLE–RELATED GENE EXPRESSION IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA

Quézia Nascimento Martins Alves, Ericka Francislaine Dias Costa, Gustavo Jacob Lourenço, Carmen Silvia Passos Lima

Universidade Estadual de Campinas, Campinas, SP, Brazil

Introduction: Oropharyngeal squamous cell carcinoma (OPSCC) is an aggressive malignancy often diagnosed at advanced stages and associated with regional lymph node metastasis. Inherited single nucleotide variants (SNVs) have been suggested to influence cancer susceptibility and tumor progression by modulating DNA repair and cellular homeostasis. Recently, our group identified an association between the AA genotype of the XPC c.2815A>C SNV and increased risk of OPSCC, as well as advanced nodal stage, but the molecular mechanisms underlying these associations remain unclear. **Objective:** To evaluate whether distinct XPC c.2815A>C SNV genotypes modulate the expression of XPC and other cell cycle-related genes in the OPSCC cell line (FaDu). **Materials and Methods:** FaDu cells were cultivated in complete Roswell Park Memorial Institute (RPMI) 1640 medium supplemented with 5% fetal bovine serum and 1% penicillin –streptomycin. FaDu cells were transfected with pcDNA3.1 expression vectors carrying either the wild-type (allele A) or variant (allele C) XPC c.2815A>C constructs, with the empty pcDNA3.1 vector used as a control. XPC expression was assessed at 24h, 48h, 72h, and 96h to confirm transfection efficiency. The 48h time point was selected for downstream analysis of the basal expression of cell cycle-related genes (CDKN2B, CCND1, CCND3, and STAT3), with ACTB used as the endogenous control. Gene expression was measured by real-time PCR, relative expression was calculated using the 2???Ct method, and statistical significance was assessed with the Student's *t*-test (p = 0.05). **Results:** Transfection with both wild-type and variant XPC c.2815A>C constructs increased XPC expression compared with the empty pcDNA 3.1 vector (control; 1.00 arbitrary unit [AU]) at 24h (8.18 and 5.59 AUs, respectively). Expression decreased over time but remained higher than control at 48h (4.88 and 3.62 AUs), 72h (3.01 and 2.40 AUs), and 96h (1.85 and 2.08 AUs). At 48h under basal conditions, cells expressing the wild-type XPC c.2815A allele exhibited higher CDKN2B mRNA levels than cells expressing the variant c.2815C allele (1.66 vs. 1.00 AUs; p = 0.05). No consistent differences were observed for the other cell cycle–related genes assessed. **Conclusion:** The present preliminary findings indicate that the XPC c.2815A>C SNV alters its basal expression as well the basal expression of CDKN2B cycle–related gene in OPSCC. Cells expressing wild-type XPC c.2815A>C A allele showed altered CDKN2B expression compared with the variant allele, indicating a potential genotype-dependent effect. Our data may provide a plausible explanation for the associations between XPC c.2815A>C SNV and risk of OPSCC and tumor behavior seen in a previous study conducted by our research group.

Keywords: XPC c.2815A>C, Pharyngeal squamous cell carcinoma, Cell cycle-related genes, Gene expression, Single nucleotide variant.

Conflicts of interest: Not declared.

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TARGETING EGFR WITH THE PEPTIDE LARLLT: IN VITRO EFFECTS ON TRIPLE-NEGATIVE BREAST CANCER AND GLIOBLASTOMA CELLS

Lucas Tetsuya Oyagawa, Danielle Vieira Sobral, Fernanda Ferreira Mendonça, Flávio Lopes Alves, Luciana Malavolta, Leonardo Lima Fuscaldi