A B S T R A C T

Introduction/Justification: CD163⁺ macrophages play a critical role in chronic inflammation, cancer, and hematologic disorders, making them a promising target for molecular imaging. These cells contribute to tumor immunosuppression, disease progression, and poor prognosis in solid and hematologic tumors. Recent studies indicate that CD163 is a relevant biomarker in Hodgkin's lymphoma, multiple myeloma, and leukemias, which are directly associated with tumor resistance and immune evasion. The cyclic peptide CTHRSSVVC has been identified as a CD163 ligand, showing high reactivity with inflammatory and atherosclerotic lesions, suggesting its potential for targeting CD163⁺ macrophages. In vitro assays demonstrated that [111In]In-DOTA-CTHRSSVVC binds to atherosclerotic plaques, further supporting its applicability in molecular imaging of inflammation and cancer. Cyclic peptides are widely used in radiotracer development due to their high specificity, enzymatic stability, and resistance to degradation. Radiolabeling of these peptides with PET radioisotopes such as 68Ga3+ and [^{18}F]AlF2+ expands their potential applications in tracking inflammatory processes and hematologic malignancies. **Objectives:** To evaluate the radiolabeling efficiency and chemical stability of the NOTA-CTHRSSVVC cyclic peptide with 68Ga3+ and [18F]AlF2+, aiming to develop a novel radiopharmaceutical for molecular imaging of CD163⁺ macrophages. **Materials and Methods:** The NOTA-CTHRSSVVC conjugate was radiolabeled [68Ga]Ga(AcO)3 or [18F]AlF2+, which were prepared in 0.2 M sodium acetate buffer (pH 4.1); reactions carried out under different peptide amounts. When necessary, the final products were purified using solid phase columns. The radiochemical efficiency was assessed by HPLC coupled with a gamma radiation detector, while chemical stability was evaluated in the labeling solution for up to 4 hours. The partition coefficient (logP) was determined in n-octanol/water system, in triplicate. **Results:** The NOTA-CTHRSSVVC peptide was successfully radiolabeled and purified with the [68Ga]Ga-NOTA-CTHRSSVVC exhibited a radiochemical purity of 97.8% (n = 3), while [18F]AlF-NOTA-CTHRSSVVC reached 95.5% (n = 3). Both radiolabeled peptides demonstrated high chemical stability, maintaining their integrity for up to 4 hours in physiological solution. The logP analysis indicated a hydrophilic profile with the value of -3.08 ± 0.16. **Conclusion:** The radiolabeling of the NOTA-CTHRSSVVC peptide with 68Ga3+ and [18F]AlF2+ was efficient and stable, demonstrating chemical feasibility for the development of a novel radiopharmaceutical. Given the potential interaction of the peptide with CD163, future investigations may focus on assessing its biological affinity and molecular imaging applications for CD163⁺ macrophages in hematologic and inflammatory diseases.

Keywords: Macrophage, Peptide, Radiolabeling, [18F]fluorine, [68Ga]gallium.

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IN VITRO POPULATION GROWTH OF HUMAN GLIOBLASTOMAS: REAL PATIENTS AND CURVE FITTING

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A B S T R A C T

Introduction/Justification: For more than a century, a variety of ordinary differential equation growth models have been used to describe and predict the proliferation of human malignancies. Indeed, in the field of mathematical oncology, the growth of cell populations over time is typically represented by sigmoidal functions, such as logistic or Gompertz curves and their generalizations. These models are particularly focused on understanding and predicting the proliferation of cancer cells, including those from human glioblastomas, which can be very aggressive brain tumors with a survival rate of less than two years. **Objectives:** This research examines in vitro cell cultures of five lines of human glioblastoma using curve fitting and numerical parameter estimation of real datasets to separately describe the growth profile of all these cell populations lineages over time. **Materials and Methods:** Cell culture experiments were performed in the Advanced Therapeutics Laboratory at FCF-UNICAMP. These included a well-established human glioblastoma cell line (NG97) and four other glioblastoma cell lines derived from clinical patients designated N07, C03, L09 and J01. Twelve repeated time series of experiments were collected for each cell line. Cell counting was performed daily on days 1 to 6. The drda R package was used for curve fitting of the measured data aiming to determine the intrinsic growth rate and other parameters for each of the five cell lines. The 5-parameter generalized logistic curve was used, and all the resulting models were analyzed under statistical criteria such as the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC). **Results:** Curve fitting analysis revealed significant diversity in the population growth of different cell lines. The drda R package proved to be highly effective in capturing these different behaviors and the unique sigmoidal shapes associated with them. Notably, the population growth of NG97 cells showed the least variability over time, with the

narrowest confidence intervals for the fitted curves and their associated parameters. This consistency can be attributed to the fact that NG97 is a well-established cell lineage. In contrast, the new patient-derived cell lines showed a greater degree of uncertainty, particularly when their confidence intervals were extrapolated beyond the last day of measurement. This observation highlights the need for additional time points in in vitro experiments with newly derived human patient cells. **Conclusion:** According to the numerical and graphical results, to AIC and BIC metrics, and also to the respective levels of provided uncertainty, the fitted models present a reasonable growth description of all the studied lineages of glioblastoma, regardless of cell line being well-established (NG97) or newly originated from human patients (N07, C03, L09, and J01). Further correlations between those results and prognostics and clinics may be of value for translational oncology.

Keywords: Generalized Logistic Function, Glioblastomas, Mathematical Oncology.

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NANOPARTÍCULAS SUPERPARAMAGNÉTICAS DE ÓXIDO DE FERRO RECOBERTAS POR COPOLIÉSTER FUNCIONALIZADAS PARA APLICAÇÕES BIOMÉDICAS

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RESUMO

Introdução/Justificativa: O câncer engloba mais de 100 tipos de doenças malignas caracterizadas pelo crescimento descontrolado de células, que podem invadir tecidos adjacentes ou se espalhar para outras partes do corpo. Há décadas, as nanopartículas magnéticas (NPMs) de óxido de ferro vêm sendo estudadas por apresentarem grande potencial para aplicações biomédicas, especialmente na oncologia, no uso de agentes de contraste para imagem por ressonância magnética no realçamento de contraste negativo nos tecidos com a presença de tumores e não tumorais, em magneto hipertermia para destruição seletiva de células cancerosas e atuando no transporte vetorizado de fármacos quimioterápicos. Independente de suas aplicações biomédicas, para evitar a aglomeração das NPMs em células, tecidos e órgãos, que pode levar a embolismos, é essencial recobri-las com materiais biocompatíveis e não citotóxicos. Poliésteres derivados de lactonas e macrolactonas, como o copoliéster poli (globalide-co-ε-caprolactona) (PGlCL), têm sido explorados devido à sua biocompatibilidade, hidrofilicidade e biodegradabilidade. **Objetivos:** Este trabalho teve como objetivo a modificação e a funcionalização do copoliéster PGICL com cisteína, a fim de atingir três objetivos associados a funcionalização das NPMs, que garantirão sua aplicação em nanomedicina, tais como: a) melhorar sua hidrofilicidade (diminuindo sua cristalinidade) para que seja carreado com mais facilidade no meio intracelular; b) permitir que grupos amina e tiol sejam pontos de ancoragem para constituírem partes de ligantes com receptores de superfície celular, tais como o ácido fólico (AF) que só são expressos em células tumorais e c) possibilitar a ligação desses grupos químicos em sistemas de "drug-delivery" com o análogo do AF, o quimioterápico metotrexato (MTX) para o tratamento de câncer de mama. Neste estudo, o PGlCL foi modificado com cisteína (PGlCL-Cys) e utilizado para recobrir NPMs de óxido de ferro (Fe3O4 - magnetita), visando futuramente em um segundo passo, a funcionalização com AF e MTX em aplicações como vetorização ativas em sistemas como "drug-delivery" e a posteriori, em ensaios in vitro de radiosensibilização em células de câncer de mama. **Materiais e Métodos:** Soluções de Fe^{3+} e Fe^{2+} em HCl. Sob refluxo, adicionaram-se H_2O aquecida, NH_4OH (30mL, pH10, 90°C), PGICL em etanol. Agitou-se 45min, purificou-se com imã, lavou-se e armazenou as NPMs. **Resultados:** A caracterização físico-química das NPMs recobertas com PGlCL-Cys foi realizada por espectroscopia no infravermelho, confirmando a presença de bandas características da cisteína (ligações C-S-C em 715,21 cm^{-1} e C-N em 1573,1 cm^{-1}) e do recobrimento das NPMs (bandas de deformação angular da ligação Fe- O em 635,63 cm^{-1} e ~590 cm^{-1}, correspondentes aos sítios octaédricos e tetraédricos da magnetita, respectivamente). A Microscopia Eletrônica de Transmissão (MET) revelou que as NPMs de Fe3O4@PGlCL-Cys possuem um diâmetro médio de 11,44 nm e exibem comportamento superparamagnético. **Conclusão:** Conclui-se que o método de coprecipitação e a síntese do copoliéster modificado com cisteína (PGlCL-Cys) foi eficaz, produzindo NPMs estáveis e monodispersas de modo que serão realizados futuramente outras caracterizações físico-químcias para avançar os estudos em ensaios biológicos in vitro para citotoxicidade e biocompatibilidade a fim de serem aplicadas no diagnóstico e tratamento de câncer de mama.

Palavras-chave: Câncer de mama, Copoliéster, Nanopartículas magnéticas, Óxido de ferro.

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APPLICABILITY OF PSMA PET/CT IN THE EVALUATION OF ADENOID CYSTIC CARCINOMA

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