# Role of N1/N2 neutrophils in regulation of tumor growth in lung cancer

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## ABSTRACT

Neutrophils display rapid and potent innate immune responses in various diseases. Tumor-associated neutrophils (TANs) however either induce or overcome immunosuppressive functions of the tumor microenvironment through complex tumor-stroma crosstalk. We developed a mathematical model to address the question of how phenotypic alterations between tumor suppressive N1 TANS, and tumor promoting N2 TANs affect nonlinear tumor growth in a complex tumor microenvironment. The model provides a visual display of the complex behavior of populations of TANs and tumors in response to various TGF-beta and IFN-beta stimuli. In addition, the effect of anti-tumor drug administration is incorporated in the model in an effort to achieve optimal anti-tumor efficacy. The simulation results from the mathematical model were in good agreement with experimental data. We found that the N2-to-N1 ratio (N21R) index is positively correlated with aggressive tumor growth, suggesting that this may be a good prognostic factor. We also found that the antitumor efficacy increases when the relative ratio (Dap) of delayed apoptotic cell death of N1 and N2 TANs is either very small or relatively large, providing a basis for therapeutically targeting prometastatic N2 TANs.

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$$\mathbf{Ma} + \mathbf{C(x)v} + \mathbf{K(x)u} = \mathbf{P}(t) \tag{1}$$

Tables and figures must be integrated with the text and numbered consecutively with Arabic numerals in the order in which reference is made to them in the text of the paper. It is recommended to place figures and tables at the top or the bottom of a page. The captions of tables and figures have to be placed above tables and below figures, respectively. There is no blank space between the caption of a table and the table, and one blank space between a figure and its caption. A table or a figure is referred to in the text as Table 1 or Figure 1, respectively, and presented as follows:

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Table or Figure

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## REFERENCES

References are to be listed at the end of the paper in the order of the reference, and are referred to in the paper by the numbers in brackets such as [1, 2]. Style the reference list according to the following examples.

1. Kim Y, Jeon H, Othmer HG. *The role of the tumor microenvironment in glioblastoma: A mathematical model.* IEEE Trans Biomed Eng. 2017;64(3):519-527.
2. Kim Y, Friedman A. *Interaction of tumor with its microenvironment: A Mathematical Model.* Bull Math Biol. 2010;72(5):1029-1068.
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5. Kim Y, Stolarska M, Othmer HG. A hybrid model for tumor spheroid growth in vitro I: Theoretical development and early results. Math Models Methods in Appl Scis. 2007;17:1773-1798.