Effect of Tuftsin on the Phagocytotic Activity of the Unicellular *Tetrahymena*. Does Primary Interaction Develop Imprinting?

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The natural mammalian phagocytosis stimulator tetrapeptide tuftsin stimulated also the phagocytosis of the unicellular *Tetrahymena*. The selectivity of the *Tetrahymena* was not complete, as threonin-free tuftsin provoked a greater response. Treatment with tuftsin did not develop functional imprinting, however the binding capacity of cell membrane significantly increased after the first treatment.

Tuftsin, a tetrapeptide (γ-globulin fraction) composed of threonine, lysine, proline and arginine, stimulates the phagocytotic activity of the leucocytes [1, 2]. Since histamine has a similar effect on the leucocytes, and also stimulates the phagocytosis of the unicellular *Tetrahymena* [3, 4], it seemed worthwhile to examine whether tuftsin, too, had an influence on the unicellular, and whether it would, like histamine, induce imprinting [3–5] at that low phylogenetic level.

Preliminary experiments performed with different (10^{-10}–10^{-5} M) concentrations of tuftsin (prepared by Dr. S. Bajusz, Institute of Drug Research, Budapest) had shown that 10^{-7} M tuftsin was most suitable for the purpose of the experiment. *Tetrahymena pyriformis* GL cells, maintained in Bactotrypton and yeast extract containing medium at 28 °C were exposed to that concentration, and were simultaneously fed Chinese ink, for 10 min, were spread on slides, dried and examined for the number of Chinese ink containing vacuoles. The mean value was calculated for each group and was related to the control value as 1 (phagocyte coefficient = PC). The Fig. 1 shows mean values calculated from five replica experiments. Cells treated for 24 h for the first time with tuftsin were examined for vacuole counts seven days later, either with or without 10-min reexposure to 10^{-7} M tuftsin. The threonine-free fraction of tuftsin was also tested for influence on phagocytosis. The intergroup differences were evaluated for significance with Student's t-test.

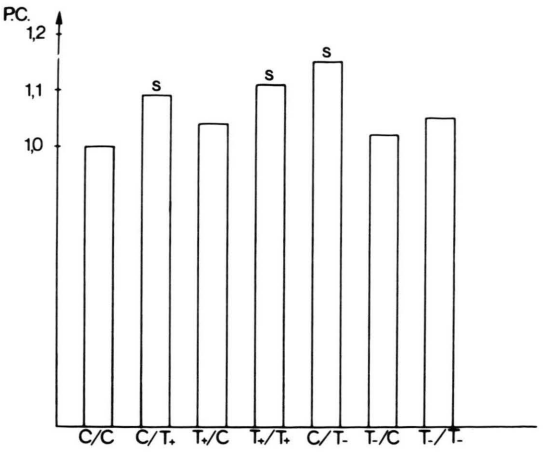

Fig. 1. Effect of tuftsin (T+) or threonine deprived tuftsin (T−) on the phagocytotic coefficient (PC) of Tetrahymena immediately after the first treatment (C/T+, C/T−) or one week after it with (T+/T+, T−/T−) or without (T+/C, T−/C) repeated treatment. Values are given as percent related to the untreated control (C/C) as 1. S = $p < 0.05$.

Tuftsin stimulated the phagocytosis of the *Tetrahymena* similarly to histamine. It follows that uni-and multicellular organisms are equally responsive to stimulators of phagocytosis. The response of the unicellular *(Tetrahymena)* is nevertheless less selective, for it showed a similar (or even greater) response to histidine in earlier studies [6], and to the threonine-deprived tuftsin fragment in the present studies, compared to the stimulant proper. Moreover, primary interaction with tuftsin or its threonine-free fragment did not durably stimulate the phagocytic activity, to judge from decline of the latter in a later stage of the experiment.

To obtain information on the imprinting potential of tuftsin, we compared the binding of FITC-labeled tuftsin between primary and second exposure. While neither tuftsin nor threonin deprived tuftsin imprinted the *Tetrahymena* for a *functional* (phagocytotic activity) *change*, the former imprinted it for a greater *binding*, to judge from a 25.1% ($p < 0.05$) increase in binding capacity at reexposure. Imprinting by the threonine-deprived fraction was more than twice as effective (55.9%, $p < 0.01$). These observations support the implication [7] that the binding and action of active molecules do not necessarily show a parallelism.

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