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*Letter to the Editor*

# Presence of Immunoglobulin G in Human Sera Binding to Carcinoembryonic Antigen (CEA) and Non-Specific Cross-Reacting Antigen (NCA)*

R. POMPECKI

*II. Medizinische Klinik und Poliklinik des Universitäts-Krankenhauses Eppendorf und Physiologisch-Chemisches Institut (Abteilung Molekularbiologie) der Universität Hamburg, Martinistrasse, 52, D-2000 Hamburg 20, Federal Republic of Germany*

IN A PREVIOUS paper carcinoembryonic antigen (CEA) binding antibodies have been demonstrated in human sera [1]. These findings proved to be consistent with those of several other studies [2–4]. Non-specific cross-reacting antigen (NCA) binding antibodies have also been shown in human sera [5]. It is important to know whether the anti-CEA and the anti-NCA antibodies are specific or not. No relationship could be found between the presence of anti-CEA and anti-blood group antibodies in our material [1]. Additionally, the NCA-binding (NCA from normal spleen, generously provided by Dr. P. Burtin, Villejuif, France) of the anti-CEA antibodies shall be communicated.

Forty-six human sera were investigated for CEA binding proteins by affinity chromatography with CEA-agarose [1]. The protein yield ranged from 10 to 50 μg/ml serum as determined by O.D. 280 absorption measurement. The samples were stored at −20°C in a concentration of 0.1 to 1.1 mg/ml protein. The CEA and NCA binding assay were performed with 10 μl aliquots of the protein preparations in 0.05 M phosphate buffer pH 7.4 containing 1 mg/ml human serum albumin. The bound antigen was separated from free antigen by absorption with *staphylococcus aureas haem.* Cowan I as previously described [6]. The maximal binding of a rabbit anti-CEA anti-serum to $^{125}$I-CEA could not be increased by addition of human binding proteins. So it is excluded that a labelled contaminant of the $^{125}$I-CEA preparation binds to the human antibodies.

The $^{125}$I-CEA and $^{125}$I-NCA binding of the human protein preparations were well correlated ($P<0.01$, Spearman's rank correlation). It was expected that some of the CEA binding antibodies would also bind to NCA since NCA has at least one antigenic determinant in common with CEA [7]. The high correlation between $^{125}$I-CEA and $^{125}$I-NCA however lead to the conclusion that most of the immunoglobulins bind to one or more antigenic determinant(s) in common for CEA and NCA. Binding proteins from individual persons with elevated $^{125}$I-CEA and $^{125}$I-NCA binding affinities were tested in inhibition assays. Excess unlabelled CEA totally inhibited the binding of both $^{125}$I-CEA (5 cases) and $^{125}$I-NCA (5 cases). While excess unlabelled NCA inhibited $^{125}$I-NCA binding (5 cases), excess unlabelled NCA could not totally inhibit the $^{125}$I-CEA binding (in 7 out of 15 cases). It seems evident that further $^{125}$I-CEA binding sites are available. Nevertheless it is possible, that an NCA excess higher than 1000-fold will inhibit the $^{125}$I-CEA binding completely. The figure

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shows typical inhibition curves for all four types.

The significance of CEA binding immunoglobulins in humans is not clear. Their cross-reactions, particularly with normal cellular antigen as it is the NCA, may be of clinical importance if they are used for diagnostic or therapeutic procedures [4].

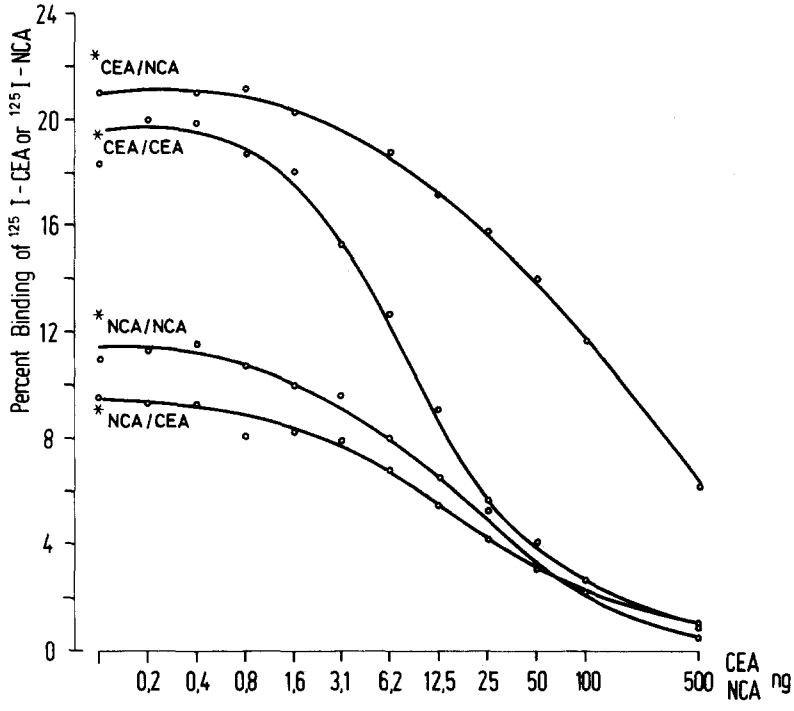


*Fig. 1. Inhibition of binding of* 0.5 ng *of* $^{125}$I-*CEA to* 10 µl *aliquots of serum proteins by increasing amounts of unlabelled CEA and NCA as well as inhibition of binding of* 0.5 ng *of* $^{125}$I-*NCA by increasing amounts of unlabelled NCA and CEA.*

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