or retinylpalmitate[5-7]. Thus retinol and retinoic acid seem to possess the same properties regarding the prophylaxis of certain epithelial tumors. Retinoic acid may be the metabolite of retinol, responsible for the latter's activity. Such a metabolic pathway of retinol has indeed been demonstrated[8,9]. Retinol would then exert its activity only after its transformation into retinoic acid. High doses of retinoic acid seem to be needed, as in a recent investigation low doses were without influence on tumor induction[10]. The mechanism of action of retinoic acid has not yet fully been elucidated. Several properties of retinoic acid may play a role in the prophylaxis and therapy of chemically induced papillomas and carcinomas. Retinoic acid may act through its effect on the growth and differentiation of epithelial tissues[11]. The prevention of metaplasia and precancerous lesions may be responsible for the lowered incidence of carcinomas. Retinoic acid may also inhibit the induction and growth of tumors by lysosomal labilization. When the lysosomal membrane is labilized[12-16], the lysosomal enzymes, released into the cytoplasm, may destroy the premalignant or the malignant cell[17]. Tumor cells could be more vulnerable than normal cells for the following reasons: The lysosomal enzymes are active in an acid milieu[18]. The tumor cell with its high anaerobic and aerobic glycolysis produces more lactic acid and has therefore a lower pH than the normal cell[19,20]. This could explain the selective sensitivity of certain tumor cells towards retinoic acid. A further hypothesis is based on the modification of the defence mechanisms. It has been shown that retinol and retinoic acid, respectively, exert an accelerating effect on graft rejection, either by an immunological or a non-immunological mechanism[21-23]. Perhaps the above-mentioned mechanisms exert a combined attack on the premalignant and malignant cell. In experimental as well as in clinical investigations the therapeutic effect of retinoic acid given either topically or systemically has been demonstrated on certain premalignant and malignant epithelial lesions[2-4,24-27]. It is rather probable, but not proved, that the mechanisms underlying the prophylactic effect on one side and the therapeutic effect on the other side are identical. It is difficult to predict whether the prophylactic effectiveness under experimental conditions has any relevance for the prophylaxis of human epithelial tumors.

Zusammenfassung. Oral verabreichte Vitamin-A-Säure besitzt bei Mäusen eine prophylaktische Wirkung auf die Entstehung von Hauptpapillomen und Hautkarzinomen, die mittels lokaler Applikation von Dimethylbenzanthracen und Krotonöl erzeugt wurden. Vitamin-A-Säure verzögert das Auftreten, verlangsamt das Wachstum und führt zur Rückbildung von Papillomen. Ferner wird die Induktion von Karzinomen gehemmt. Diese treten bei prophylaktischer Verabreichung von Vitamin-A-Säure verzögert und in deutlich verringerter Anzahl auf. Der Wirkungsmechanismus wird diskutiert.

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Antigenic Variation of the Avian Myeloblastosis Virus Obtained from Chick Embryo Fibroblasts

Avian Myeloblastosis Virus (AMV) is structurally complex[1] and would be expected to contain several antigens. This virus which causes leukemia in young chickens is released from the surface of the circulating leukemic myeloblasts and is shown to contain ATPase and RNA digesting enzyme of cellular origin in its constitution which are lacking when the same virus is produced by chick embryo fibroblasts (CEF)[2]. CsCl density gradient centrifugation also revealed a difference in the density of the myeloblast and fibroblast virus of AMV[3]. It was then of interest to see whether an antigenic variation of the AMV can be obtained from myeloblast and fibroblast cells. Viruses obtained from both these cells were analyzed in an immunoelectrophoretic system with the antisera produced against Tween-Ether (TE) split viral products of myeloblast AMV, and it is shown that there is an antigenic variation in the AMV produced by myeloblast and fibroblast cell.

Myeloblast virus was recovered from the blood plasma of infected chickens diseased with myeloblastic leukemia[4]. Plasmas were pools of several birds containing about 5×10^{11} virus particles per ml as estimated by particle count[5]. Fibroblast virus was obtained from the

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supernatant fluid collected between 3rd and 5th days post infection of primary cultures of RIF-free chick embryo fibroblasts[6] inoculated with a multiplicity of 100 myeloblast AMV particles per cell. Supernatants so obtained contained around 3×10^9 virus particles per ml. Both types of viruses were purified in a similar way by 4 alternate low and high speed centrifugations[7]. The purified viral pellets were treated with TE as described by ECKERT et al.[8] prior to use as immunogens or test antigens. All preparations of disrupted virus were exhaustively dialyzed against phosphate buffered saline (pH 7.4).

Rabbits were given an initial inoculation of detergent treated myeloblast virus of 10^{12} particles emulsified either in Freund's incomplete or complete adjuvent. Booster injections were given 5 weeks following primary immunization and consisted of 5×10^{11} disrupted particles prepared in a similar way. All inoculations were in the hind foot pads. The rabbits were bled from the ear 4 weeks following primary immunization and 10 days following booster injections. Serum was stored at -20 °C.

Gels were prepared with 1% noble agar on microscopic slides. 10 µl of antigen preparations were added into the slots and electrophoresis carried out with 0.1 *M Tris* buffer at pH 8.0 for 50 min. Following the electrophoresis a trough was cut in the middle of the slide and 100 µl of the antiserum was added. The slides were incubated at 37 °C for 24–72 h before reading. They were then washed for 1–2 days and stained with amido black. The stained preparations were then photographed.

The Figure shows precipitin lines obtained with both virus preparations when reacted against the rabbit antiserum. While myeloblast AMV split products gave 4 lines of reaction, the fibroblast virus showed only 2 lines. These 2 precipitin lines present in the fibroblast virus, however, show identity of reaction with the corresponding lines of myeloblast virus. The remaining 2 lines of myeloblast virus, of which one is prominent and migrates towards cathode, and another faint one are absent in the fibroblast virus split products.

Earlier studies have used complement fixation (CF) to determine the number of antigens present in the AMV[8]. Since CF test is limited in its ability to distinguish the number of antigens contributing to a positive reaction, we have employed immunoelectrophoresis to demonstrate precipitating antigens contained with in the disrupted virus preparations. In a similar study but using avian tumor group specific antisera from Rous sarcoma tumour bearing hamsters, it was shown that SDS treated AMV contains 3 antigenic components[9]. Our studies confirm that multiple antigenic components are present in AMV.

In a comparative study of the viral antigens present in the AMV infected myeloblast and fibroblasts, it was shown that chick tissue components of the virus present in the myeloblast cell are absent in the fibroblast cell[10]. A similar difference is now indicated by the AMV produced by these 2 different host cells. These two studies and those already mentioned clearly demonstrate that AMV incorporates cellular material, as it buds from the surface of a host cell, and in this respect AMV produced by different host cells shows variation in its constituent components of cellular origin.

Zusammenfassung. Immunelektrophoretisch wird ein verschiedenes Verhalten des Vogel-Myeblastosis-Virus nachgewiesen, je nachdem, ob dieses in Myeloblasten oder in Fibroblasten gezüchtet wurde.

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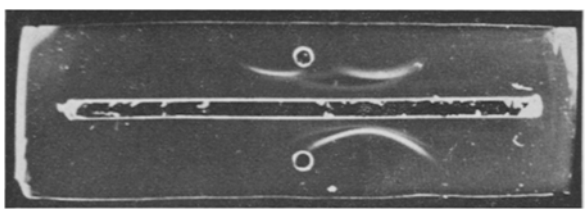

Immunoelectrophoresis of TE split AMV from myeloblast (upper well) and fibroblast (lover well) cells. The trough contained rabbit antiserum of AMV split products. Precipitin lines migrating towards cathode present in the myeloblast AMV are absent in the fibroblast AMV.

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Isolation and some Properties of the Heparin-Neutralizing Factor (PF 4) Released from Human Blood Platelets

A heparin-neutralizing activity in extracts from blood platelets, subsequently termed platelet factor 4 (PF 4), has been described as early as 1951 by VAN CREVELD and PAULSSEN[1]. First attempts at characterizing this material were made by DEUTSCH et al.[2,3], who finally obtained by chromatography on DEAE-Sephadex A-50 a 950-times enriched product. These and other studies, in particular by POPLAWSKI and NIEWIAROWSKI[4], as well as by FARBISZEWSKI et al.[5] led to the assumption that PF 4 is a protein of relatively low molecular weight or a large polypeptide[6]. In recent years it has been found that PF 4 may interact with fibrinogen and certain fibrinogen-complexes and in this form may contribute to platelet aggregation[7,8] and play a role in intravascular coagulation[9]. Therefore a more detailed study of some of the properties of purified PF 4 seemed justified.

Since PF 4 is released by thrombin from platelets in a fast reaction[10] it seemed appropriate to use the supernatant from thrombin-treated platelets as the starting material for its isolation, the more as the specific activity of the released material as calculated on a protein basis is up to 20 times higher than that of homogenized platelets.

Platelet factor 4 activity was determined according to a slight modification of the method by HARADA and ZUCKER[11]. Platelets were isolated from the buffy coats of