Fluorescent Mast Cell in Precancerous Mouse Skin

One of the results of painting the skin of mice with tar or a carcinogenic hydrocarbon is the gradual development of a mast cell reaction in the altered dermis[1]. Despite some evidence to the contrary[2], such mast cells are said to exhibit a golden-brown fluorescence in ultra-violet light[3].

While investigating this problem, using fresh tissue spreads or frozen material unfixed in any other way, it was observed that the golden-brown fluorescence appears in the mast cells of the precancerous dermis only after treatment with formalin, and that a non-fluorescent precursor substance can be extracted from the mast cells by prolonged immersion of the tissue in acetone.

Since we[4] have recently confirmed the findings of others[5] that the mast cells of the mouse (and rat) are exceptional in containing not only histamine, but also 5-hydroxytryptamine (5-HT), it seemed of interest to discover whether the fluorescent material in precancerous skin is 5-HT which can be converted into a fluorescent β-carboline derivative by the action of formaldehyde[6].

Twenty four stock mice of either sex were painted twice, 7 days apart, along the entire length of the back with an 0·5% solution of 9,10-dimethyl-1,2-benzanthracene in acetone. 3 months later the mice were killed and the treated portions of skin excised. Vertical and horizontal frozen sections, free-hand sections and tissue spreads prepared from dermal scrapings, with or without additional fixation in 10% formalin, were examined under the microscope in ultra-violet light and then stained either with toluidine blue for mast cells, or with acetylated Sudan black for phospholipids[7]. These histological experiments confirmed that most of the golden-brown fluorescence in the mast cells of precancerous mouse skin is due to the action of formaldehyde on a substance which can be extracted with acetone. Treatment with acetone did not affect the ability of the granules to stain with either toluidine blue or with acetylated Sudan black.

The chemical identity of the fluorescing substance was arrived at as follows. Dermal scrapings from ten other treated skins were homogenized in acetone, and the extract was concentrated *in vacuo*. Fats were removed with petroleum ether. The final extract, when treated with formaldehyde, exhibited a golden-brown fluorescence in ultra-violet light, similar to that seen in the tissues, and having its maximum around 2800 Å. Further extraction of the skins with fat solvents failed to yield additional material giving the characteristic fluorescence. Chromatographic examination of the original acetone concentrate, as described in detail elsewhere[4], indicated that the fluorescing substance is 5-HT.

There is now ample evidence that mast cells in general are rich in histamine[8]. Just why the mast granules of the mouse and rat manufacture or store a second amine, 5-HT, is unknown. Work is in progress to trace the source of this 5-HT which, in the mast cells of precancerous mouse skin, reaches a concentration normally achieved only by the cells of the enterochromaffin system[9].

The possibility remains that some, at least, of this 5-HT is derived, directly or indirectly, from the precancerous epidermis itself and that the elucidation of the problem may shed light on a chain of events, which, in the mouse (and rat), is prone to end in the development of cancer.

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Résumé

L'application d'un hydrocarbure cancérigène à la peau de la souris est suivie d'une mastocytose très nette qui évolue dans le tissu conjonctif. Après traitement au formaldéhyde d'une coupe gelée, quelques mastocytes prennent au microscope à fluorescence une couleur brun doré. Par essai direct et par chromatographie sur papier, on a constaté que la substance fluorescente est le dérivé β-carboline de la 5-hydroxy-tryptamine.

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Beobachtungen über Fälle von frühzeitiger Trächtigkeit bei der Albino-Maus

Die Geschlechtsreife der weiblichen Albino-Maus kündet sich durch verschiedene Erscheinungen an: Eröffnung des Vaginalverschlusses, erster Oestrus, erste Begattung, erste Trächtigkeit. Diese Erscheinungen treten nicht ganz gleichzeitig auf und bedingen einzeln noch nicht die volle Geschlechtsreife. Der Vaginalverschluss wird bei der Maus nicht, wie vielfach angegeben wird[1], durch eine Membran gebildet, sondern durch einen weit in die Vagina hineinragenden soliden Gewebepfropf (Bloch[2]), Abbildungen 1 und 2. Die ersten Begattungen führten nach Mirskaia und Crew[3] nur in 24% der Fälle zur Trächtigkeit, während bei 3–6 Monate alten Weibchen der Prozentsatz 80–90 betrug. Da die jungen Mütter oft den ersten Wurf fressen oder selber bei oder unmittelbar nach dem Wurf sterben, nehmen diese Autoren an, dass der jugendliche Organismus für die Produktion und Aufzucht der Jungen nicht reif ist, und definieren die Geschlechtsreife als die Fähigkeit, lebensfähigen Nachwuchs zu erzeugen und aufzuziehen. Dass die erste Aufzucht oft nicht gelingt, konnte ich bei der Maus häufig beobachten.

Kirkham[4] gibt für die Geschlechtsreife der Maus 6 Wochen an, Parkes[5] für die Eröffnung der Vagina das Ende der 7. Woche, für die erste Ovulation den 56. Tag. Engle

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