was attributed to the lack of a peptide portion[10,11]. The results reported here suggest that the peptide-containing and wax D-similar active fraction, LF, from BCG was incorporated into the cellular structure in such a manner that it can only be extracted after the whole cells of BCG have been treated with diluted acid in a suitable organic solvent mixture.

The loss of adjuvant activity of BCG after extraction of LF suggests that LF is the only adjuvant fraction present in the bacillus. Nevertheless, BB–LF together are more active than LF alone. LF is a free molecule, its moderate adjuvanticity may be due in part to its rapid elimination. The BB–LF aggregate appears to be constituted with an adjuvant agent, LF, located on the bacterial body, BB. This latter has no adjuvant activity but it probably acts as an immunological carrier which protects the adjuvant molecule and delivers it to adjuvant sensitive cells.

*Résumé.* Une fraction peptidoglycolipidique peut être extraite à partir du BCG par décapage acide dans un mélange de solvants fortement lipophiles. Cette fraction appelée «LF» peut reproduire l'activité adjuvante du BCG entier dans les réactions immunitaires à médiation cellulaire et humorale. L'activité adjuvante du BCG apparaît comme liée à ce composant actif, LF, car après son extraction, le résidu bacillaire (BB) est dépourvu d'activité adjuvante. Néanmoins lorsque BB est utilisé pour adsorber («véhiculer») LF, le complexe BB–LF s'est révélé le meilleur adjuvant.

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## Colostrum-Cell and Leucocyte Associations in Man

The origin of colostrum cells has been controversial since their cellular nature was first postulated in 1847[1]. Such cells possess finely vacuolar cytoplasm and sharp cell margins (Figure), and are widely found in undrained mammary secretions (colostrum)[2]. Numerous studies of the cells[3–6] in man, domestic ungulates, and laboratory rodents have yielded conflicting views as to whether the colostrum cells are derived from mammary epithelium or from infiltrating leucocytes.

Colostrum cells in duct which is surrounded by small-round-cell infiltrate. Haemalum and eosin. ×150.

Benign mammary dysplasia[7], a common disease of the breast in women, often features accumulation of undrained mammary secretion and of colostrum cells. In view of its variable morphology and the large number of lesions available for study, the condition is well suited to investigation of the relationship between colostrum cells and inflammatory cells that may be found in the lesions. The three inflammatory cell-types found in periductal tissue considered here are: small round cells[8] with inconspicuous cytoplasm, cells with ochre cytoplasmic pigment (ochrocytes)[9], and cells with prominent foamy cytoplasm lacking pigment (foam cells)[10].

An unselected consecutive 4-year series of 212 benign mammary dysplasias from women over the age of 40 years received in the University Department of Histopathology at the Bristol Royal Infirmary was studied. The tissues were fixed in buffered 10% formalin and embedded in paraffin wax. Haemalum and eosin-stained sections of lesions from which at least 2 paraffin blocks had been prepared were systematically examined in a rectilinear pattern. Each lesion was assessed for the presence or absence of colostrum cells in the ductal secretions, and independently, for the presence or absence of ochrocytes, and small round cells and foam cells in a band exceeding 0.125 mm radial width in the periductal connective tissue.

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The distribution of the 212 cases arranged according to the presence or absence of the cell-types in a four-dimensional contingency table is shown in Table I. Since the unrestricted sampling corresponds to Model 1 of LANCASTER[11], the analysis of the associations (first-order interactions) between the pairs of cell-types, and of the higher-order interactions were performed according to that method. All the associations between the pairs of cell types (Table II) were highly significant. No second-order interaction was significant, but the third-order interaction (C-O-S-F) was of possible borderline significance. The interpretation of such higher-order interactions is often difficult, but in this instance the largest contributions to the overall $\chi^2$ were from the boxes in which all four cell-types were either present or absent. The excessive numbers observed in these boxes represent a tendency to an all-or-none phenomenon that is reflected in the third-order interaction.

Table I. $2^4$ contingency table showing numbers of benign mammary dysplasias with and without colostrum cells and periductal leucocytes

| Colostrum cells present (+) | | | | | | |
|---|---|---|---|---|---|---|
| SRC[a] | absent | (−) | | SRC[a] | present | (+) |
| 5 | 0 | + | | + | 39 | 20 |
| 12 | 0 | − | Ochrocytes | − | 35 | 7 |
| − | + | | | | − | + |
| Foam cells | | | | Foam cells | | |
| **Colostrum cells absent (−)** | | | | | | |
| SRC[a] | absent | (−) | | SRC[a] | present | (+) |
| 0 | 0 | + | | + | 2 | 1 |
| 44 | 1 | − | Ochrocytes | − | 44 | 2 |
| − | + | | | | − | + |
| Foam cells | | | | Foam cells | | |

[a] SRC = periductal small round cells.

Table II. Significances of associations and higher-order interactions (calculated from data in Table I)

| Interaction | | $\chi^2$ (d.f.) | |
|---|---|---|---|
| Colostrum cells (C) | – Ochrocytes (O) | 63.07 | (1)[a] |
| Colostrum cells | – Small round cells (S) | 28.31 | (1)[a] |
| Colostrum cells | – Foam cells (F) | 14.53 | (1)[a] |
| Ochrocytes | – Small round cells | 22.46 | (1)[a] |
| Ochrocytes | – Foam cells | 21.93 | (1)[a] |
| Small round cells | – Foam cells | 11.89 | (1)[a] |
| 2nd-order interactions: | C-O-S | 0.02 | (1)[c] |
| | C-O-F | 1.24 | (1)[c] |
| | C-S-F | 0.54 | (1)[c] |
| | S-O-F | 1.79 | (1)[c] |
| 3rd-order interaction: | C-O-S-F | 6.18 | (1)[b] |
| Total $\chi^2$ | | 171.96 | (11) |

[a] $p < 0.001$; [b] $p < 0.025$; [c] not significant.

The findings that colostrum cells in non-neoplastic human breast tissue are closely associated with small-round-cell, ochrocytic and foam-cell infiltrates, and that all these cell-types themselves are mutually associated, is not due to second-order interactions. Nevertheless it is possible that the weak third-order interaction may have contributed to the observed first-order associations. Naturally, mere association is no proof of a common histogenetic origin of these cells. However the similar fluorescent and staining characteristics of colostrum cells and ochrocytes[8,12], and the tendency of colostrum cells, ochrocytes and foam cells to show multinucleate forms[8–10] suggest similar functional characteristics. It should be noted that none of these morphological similarities is likely to have produced a selectional bias in the assessment of the presence or absence of the cell-types.

The mutual associations found here, together with the shared morphological characteristics and active phagocytic capacity of human colostrum cells[13], support the view that most cells in all four categories are of macrophage nature. Possibly colostral secretion itself contains an irritant that attracts the cells into its vicinity. The slight tendency to an all-or-none response would accord with reaction to such a stimulus.

*Résumé.* L'étude de 212 biopsies de la maladie fibrocystique du sein humain montre des associations fortes et mutuelles entre les cellules du colostrum les petites cellules rondes, les ochrocytes et les cellules écumeuses qui se trouvent dans le tissu conjonctif entourant les canaux du sein. Une analyse statistique multidimensionelle ne fait pas apparaître une interaction de second ordre entre les combinaisons des facteurs. Mais il y a une faible interaction de troisième ordre, dont une explication possible est une réponse inflammatoire des quatre types de cellules à un stimulant irritant du colostrum lui-même.

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## Uterine Secretion During the Sexual Cycle in the Rat and its Capacity to Disperse Corona Cells in vitro

In recent years, increasing attention has been devoted to the role of the secretions of the genital tract, especially in relation to the fecundation process and particularly concerning the viability and behaviour of the gametes (HOMBURGER and TREGIER[1]) and the implantation of the blastocyte (CLEMENTSON et al.[2]; DICKMAN[3]). Many different kinds of investigation have been undertaken in this field. It has been found that the secretion accumulating in the closed uteri of spayed, oestradiol-primed rats has the ability to disperse the corona cells of the ova in vitro (MEGLIOLI and DESAULLES[4]). Because of the difficulty of collecting enough of this secretion for quantitative analysis and assay, especially from small experimental animals, such as rats and mice, it has proved