Adstock Science Club

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PhD student/Research Assistant

Clore Laboratory

University of Buckingham

My Background…

- Finished school education in India
- Completed A-Levels in London
- BSc Biotechnology (2005-2008), University of Westminster
- MSc Molecular Genetics (2008-2009), University of Leicester
- Research Assistant (2010-), University of Buckingham
- On going PhD in Biomedical Science (2011-), University of Buckingham

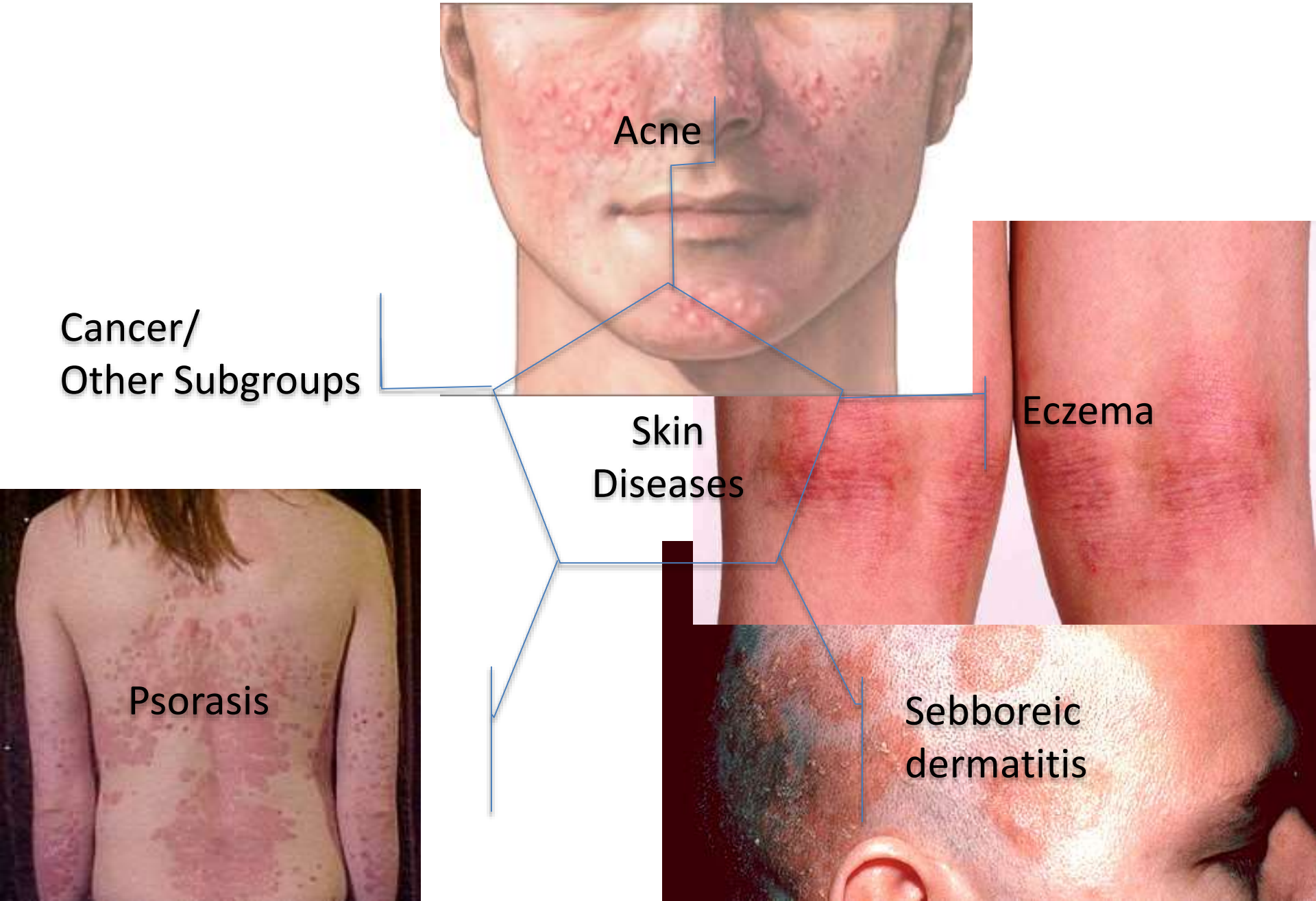
Clore Laboratory, University of Buckingham

- Internationally recognized research group
    - Led by Prof Mike Cawthorne and Prof Jon Arch
    - Track record in drug discovery, including insulin sensitizer rosiglitazone

- Main focus of the lab: physiology of metabolic diseases, particularly diabetes and obesity

- Our group: research focused on skin complications
    - Molecular aspects of dermatological states
    - Understanding skin integrity in diabetic and obese animal models
    - Understanding the role of human dermal fibroblast in processes such as wound healing, ageing etc.
    - Understanding the etiology of a rare disease

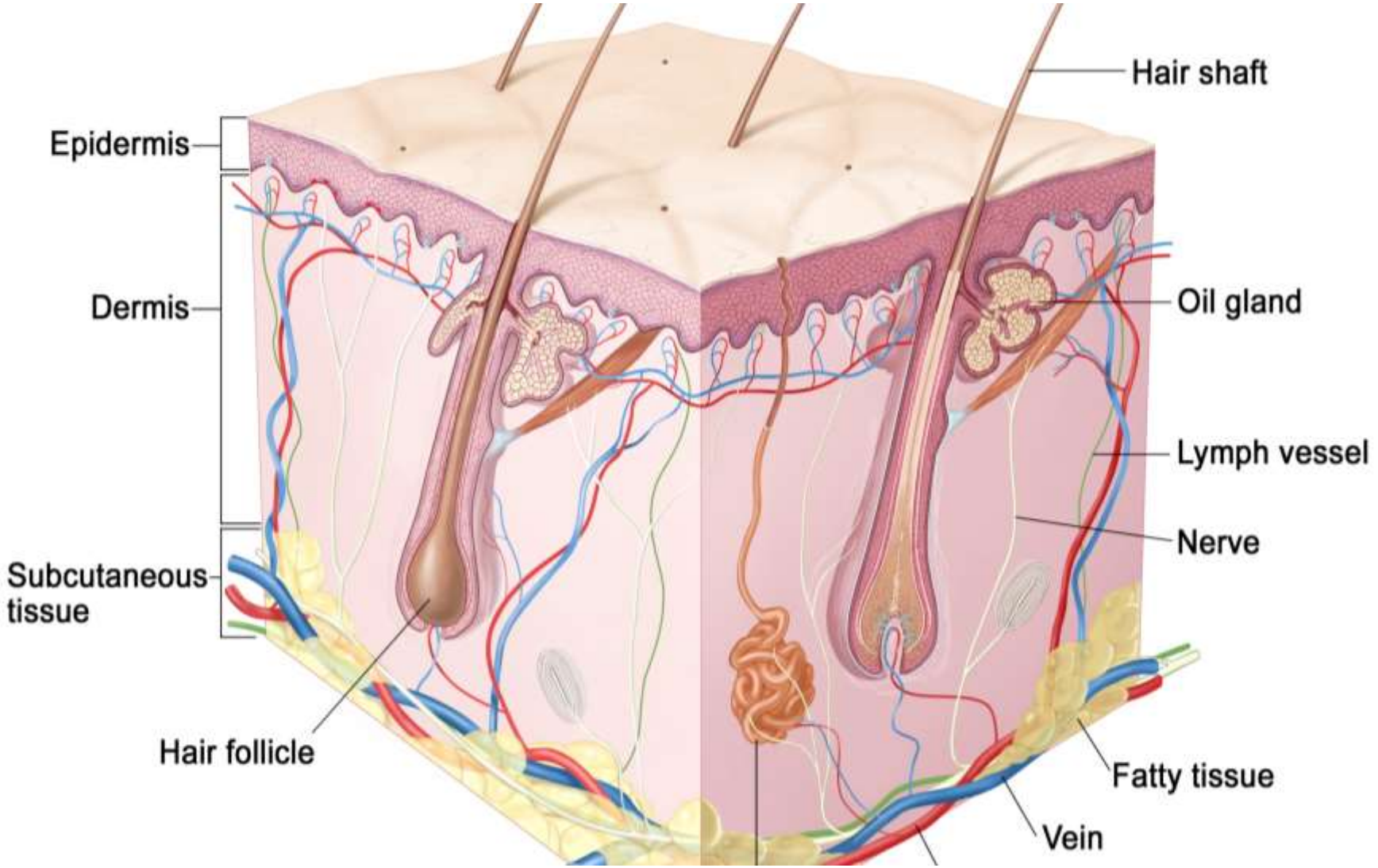
Topic of interest: Cutaneous Complications



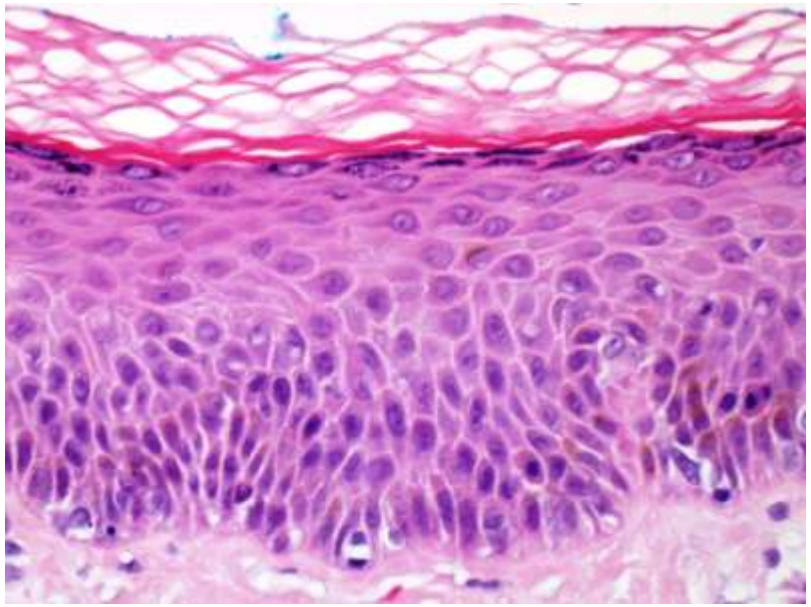
Squamous Cell Carcinoma

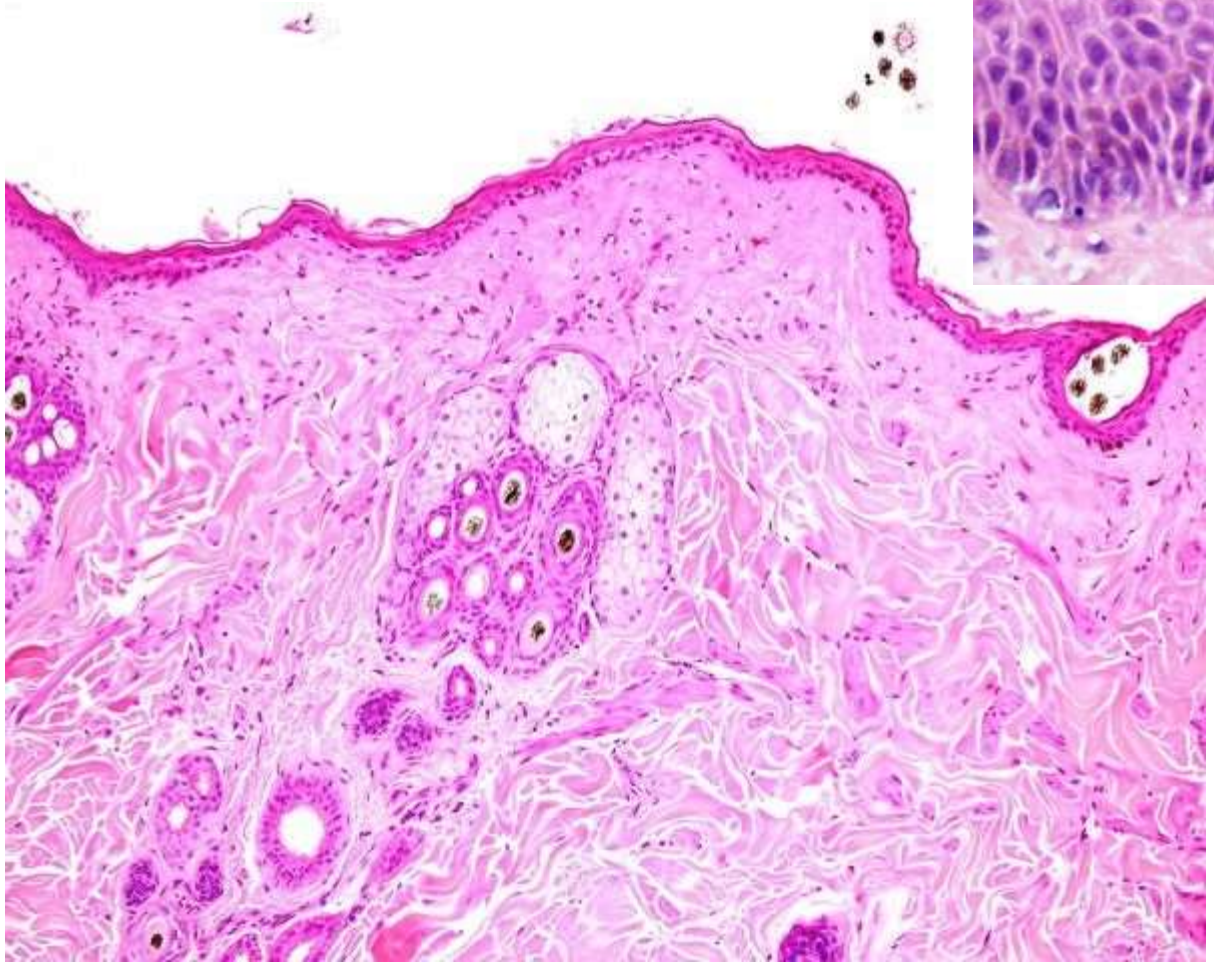
Disease of interest: Langerhans Cell Histiocytosis (LCH)

Organ/Tissue of Interest: Skin

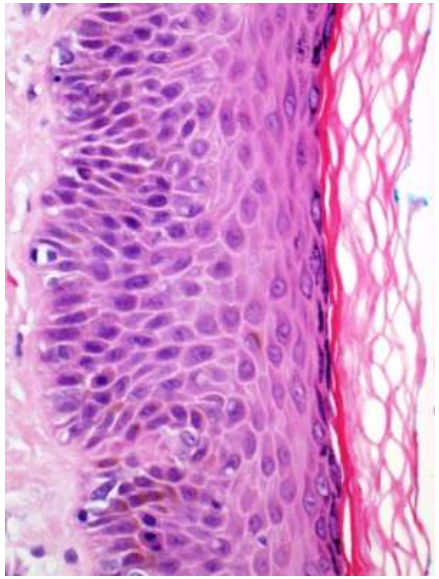


Normal Skin Histology



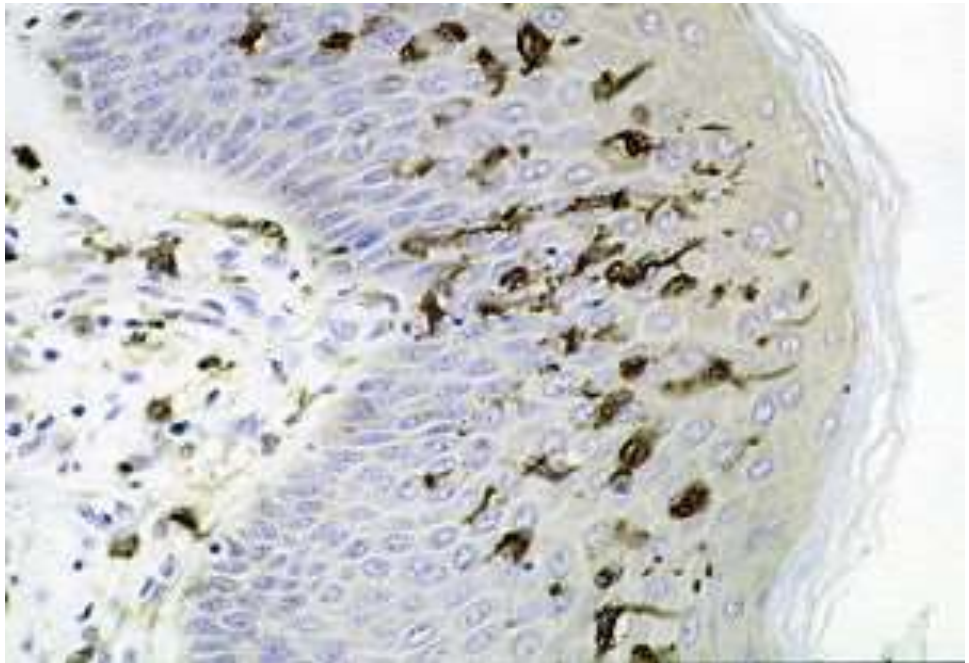


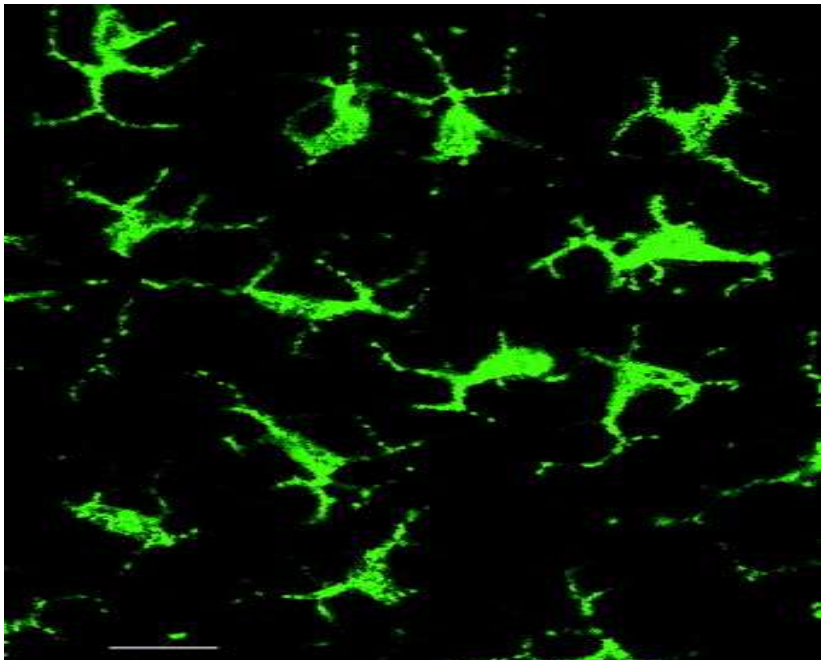
Cell of Interest: Langerhans cell



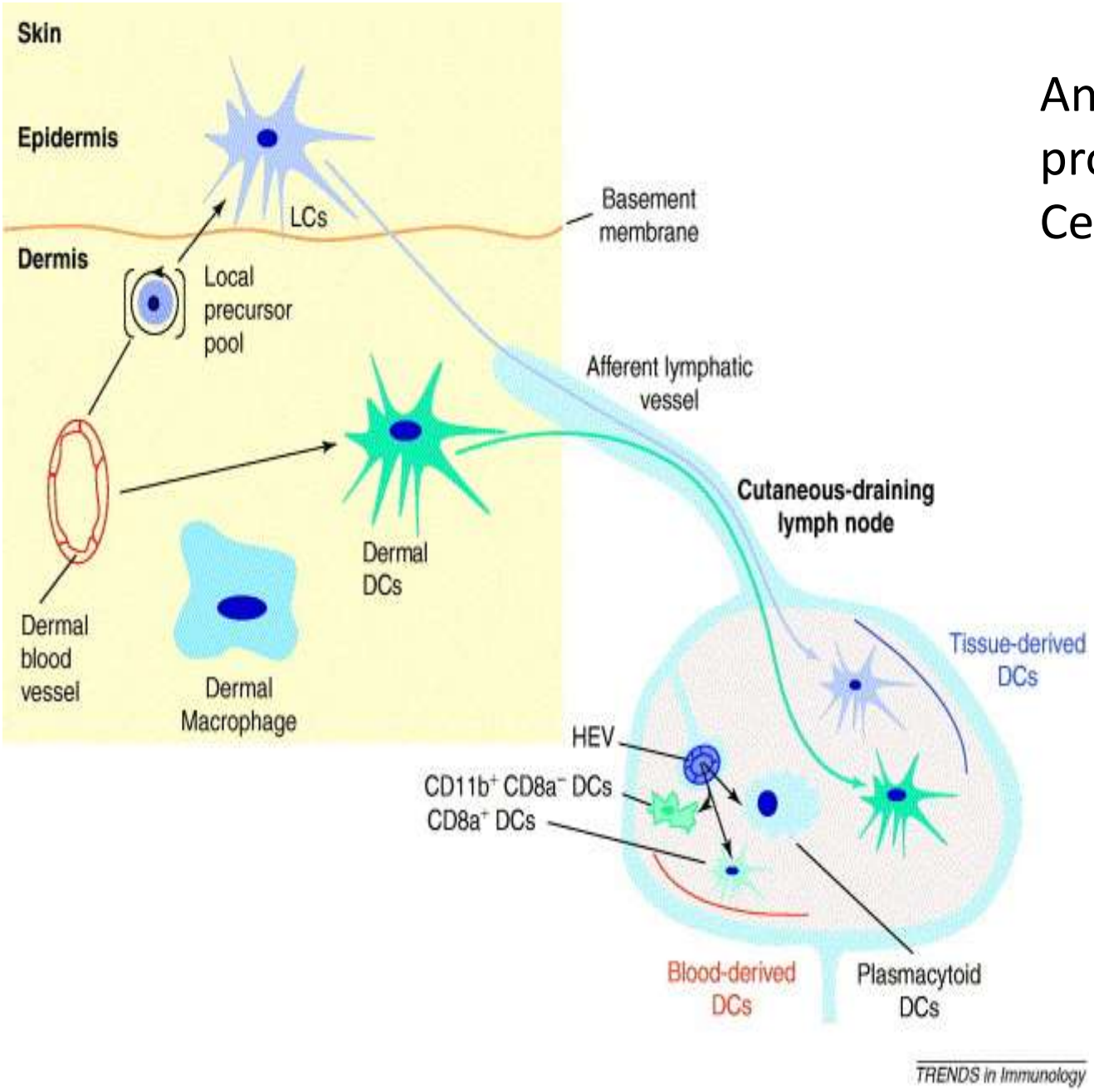
Normal LC

- Migrant of bone marrow origin
- Reside in the epidermis
- 2% of epidermal cells
- Dendritic, professional antigen presenting cell of the skin





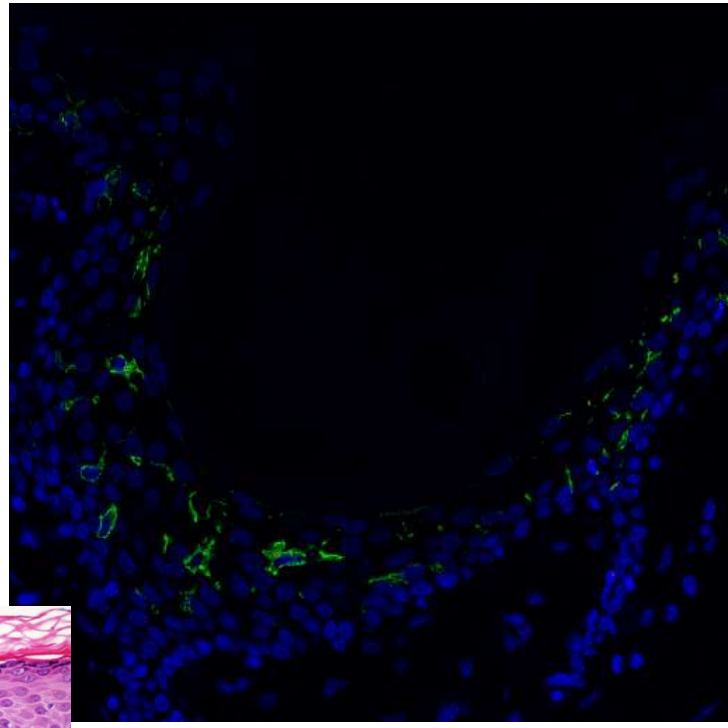
Antigen presenting process of Langerhans Cell

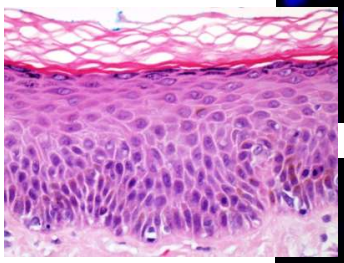


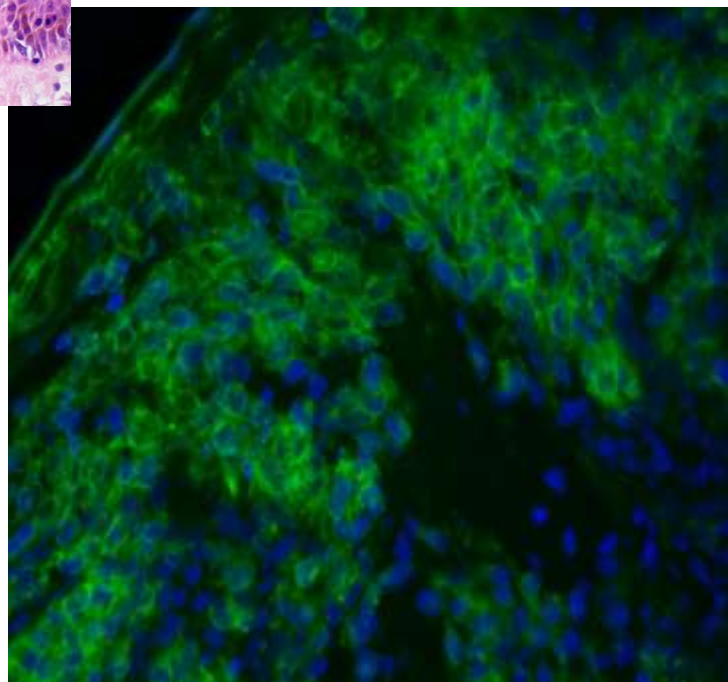
Langerhans Cell Histiocytosis (LCH)

- LCH is a rare and potentially fatal disorder of unknown aetiology
- Overall incidence of LCH is estimated at 1 per 2 million children/ developed countries the estimates are higher at 2 per 200,000 births
- LCH can be observed in both infants and adults
- Disease Stage: Single system disease , Multisystem disease, Multisystem disease with evidence of vital organ dysfunction
- Skin involvement in LCH in adults is common and may be the first or only organ involved

- LCH is not only found where LC are physiologically present:
    - LC – epidermis/dermis, lymph nodes, bronchial epithelium, thymus
    - LCH – skin, bone, lymph node, lung (in smokers), pituitary, liver, spleen, GIT, meninges, CNS
- LCH is characterised by the abnormal accumulation of CD1a-positive cutaneous Langerhans-like cells in various body sites, including skin
- Tissue damage and morbidity results from lesional cytokine release







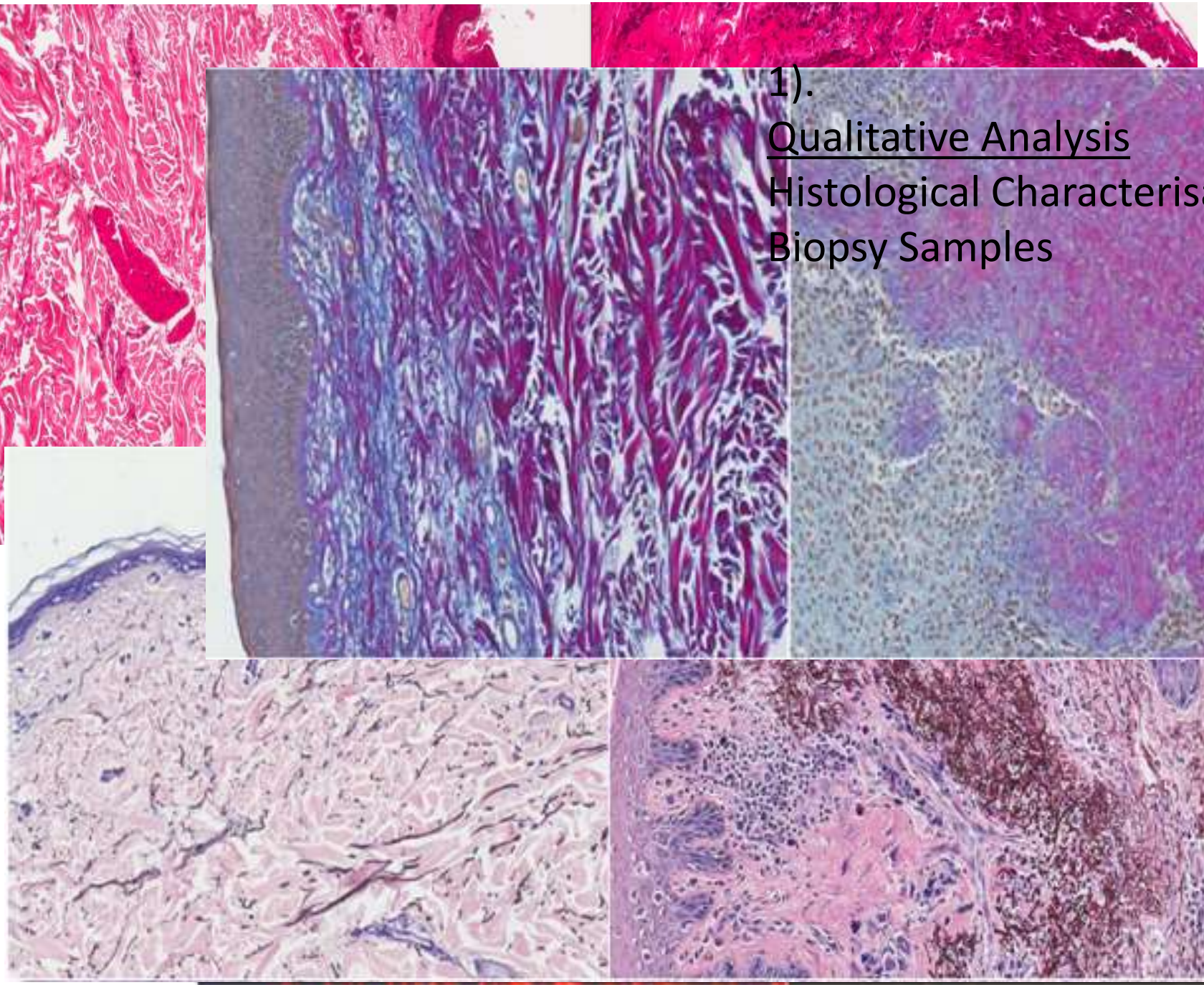
Problems faced in LCH research

- Exact aetiology and pathogenesis remains unclear
- Disease probably under-reported due to difficulties in diagnosing the disease
- No prognostic biomarkers to facilitate disease stratification are known
- Treatment protocols vary between centres
- Studies hampered by scarcity of samples and lack of models

Project Aims

- To provide diagnostic and prognostic markers of LCH for the clinic
- To provide a 'fingerprint' of genes that can differentiate between the different LCH classifications to provide guidance for treatment
- To provide insight into the aetiology underlying LCH through gene expression analysis

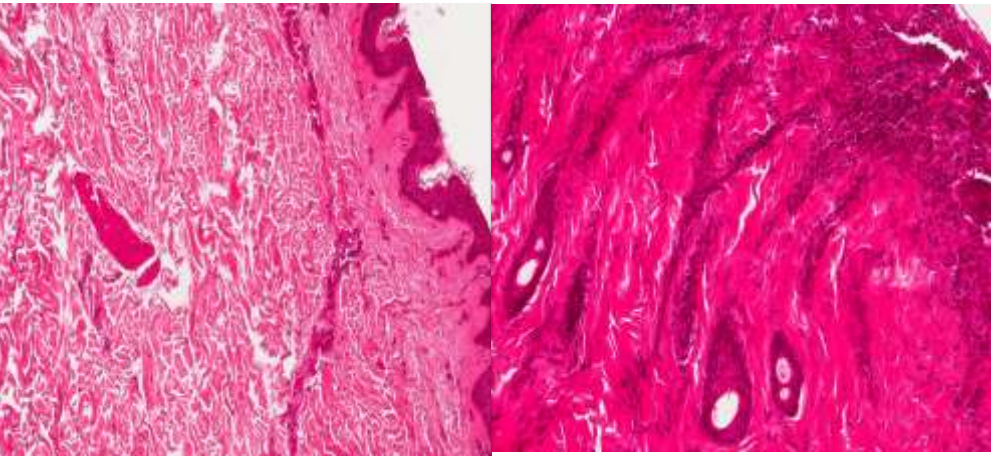
How are we approaching the problem??



1).

Qualitative Analysis

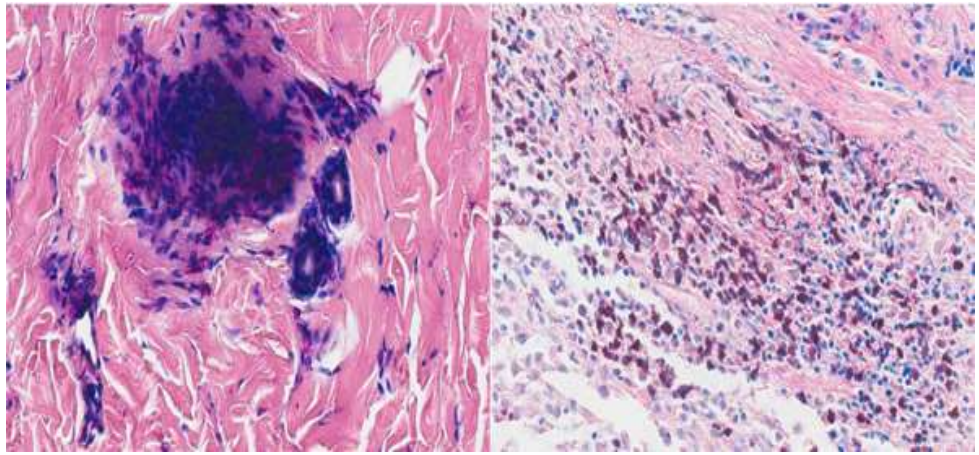
Histological Characterisation of Biopsy Samples

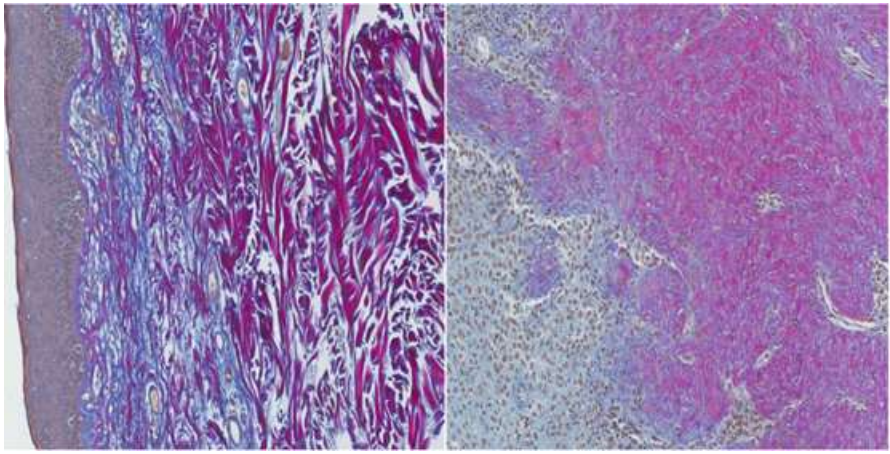


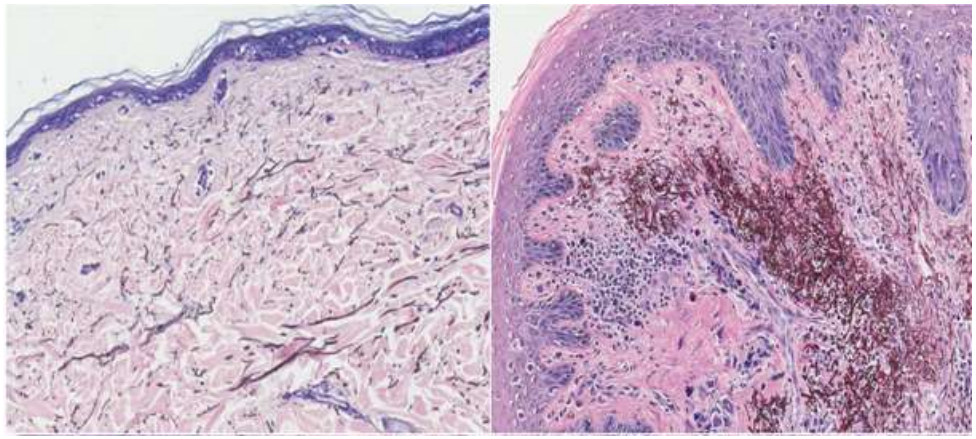
1).

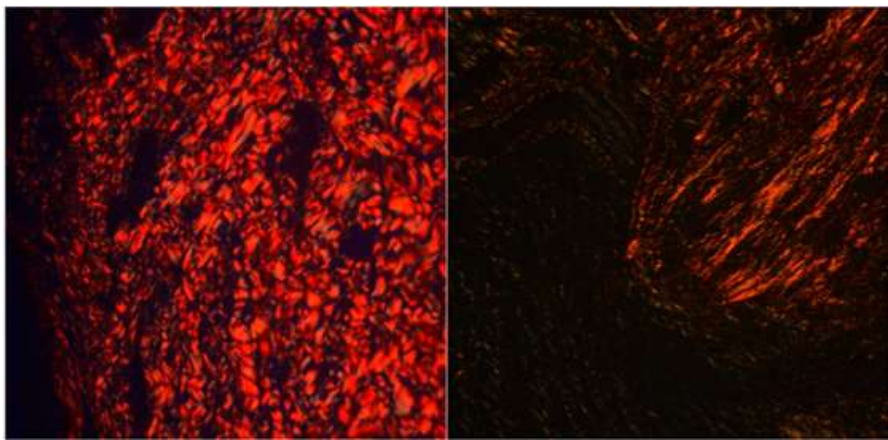
<u>Qualitative Analysis</u>

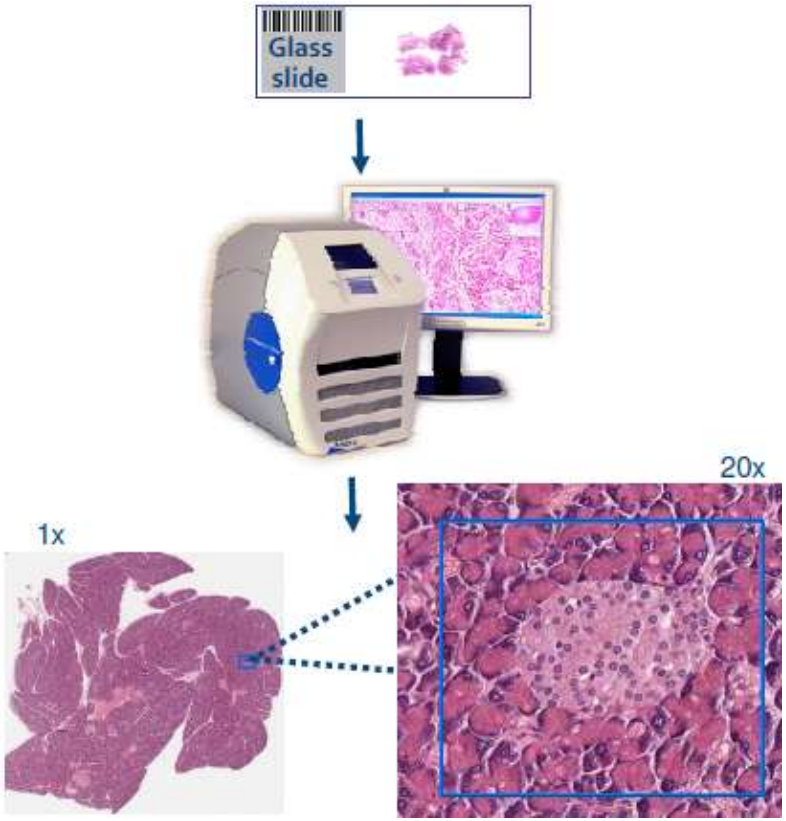
Histological Characterisation of Biopsy Samples







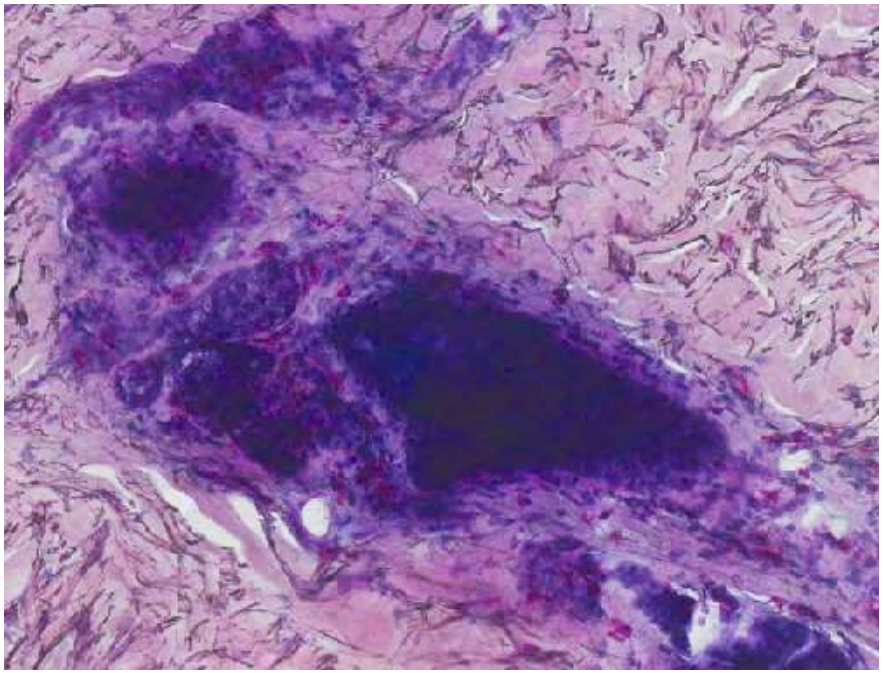


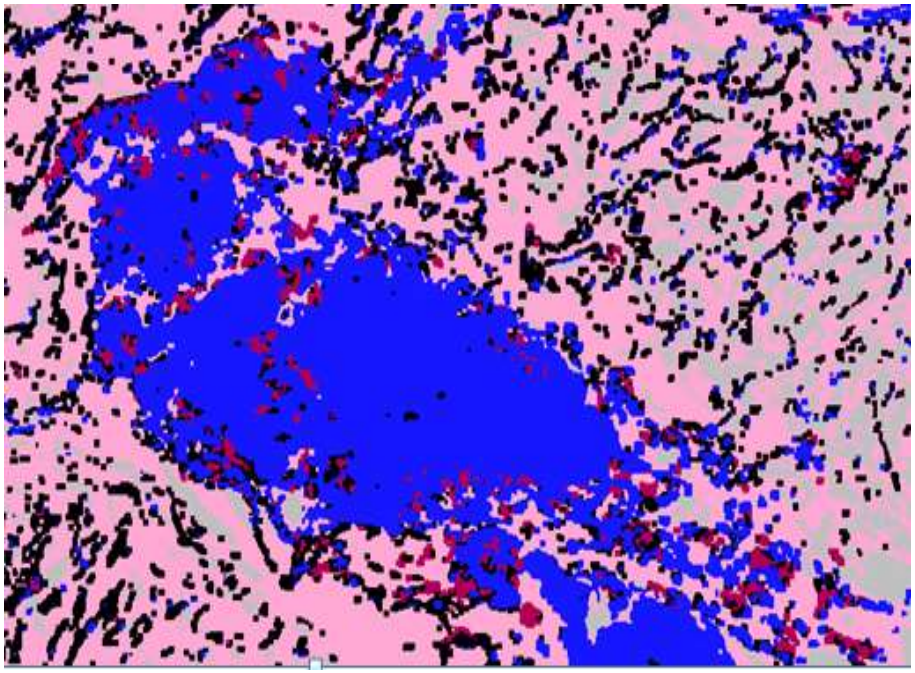


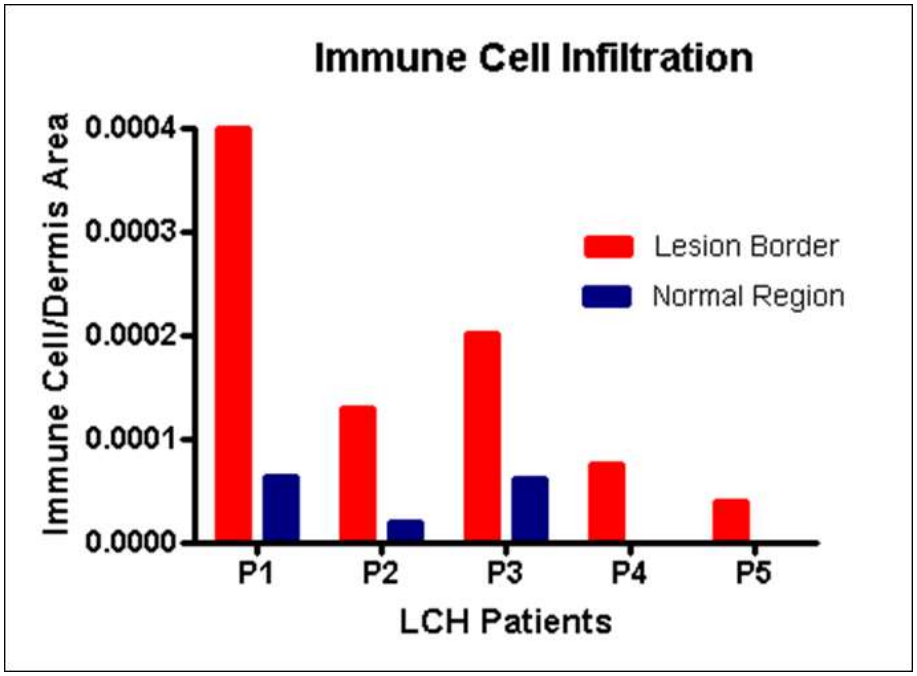
2).

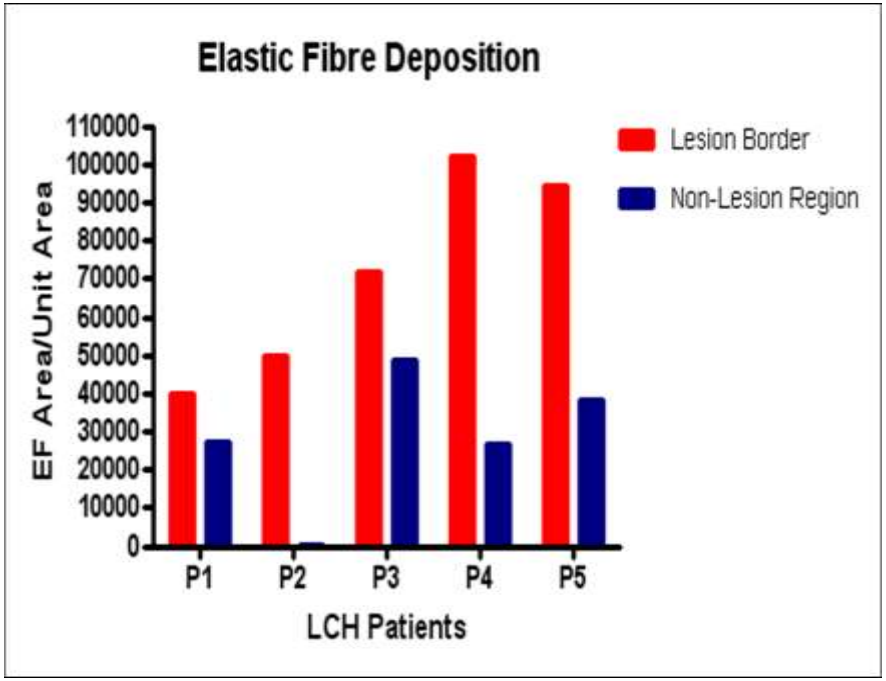
<u>Quantitative Analysis</u>

Using Image Analysis

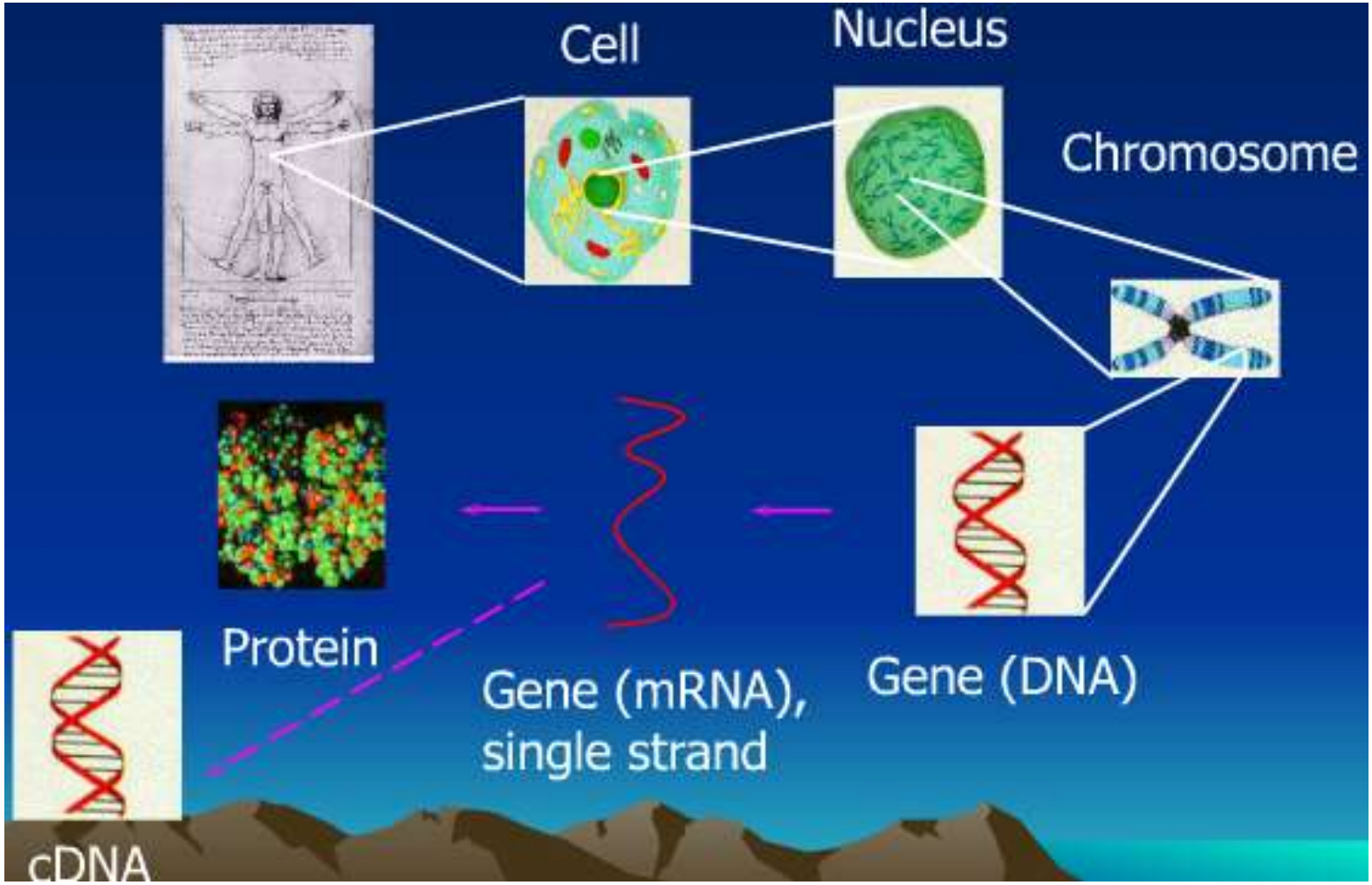




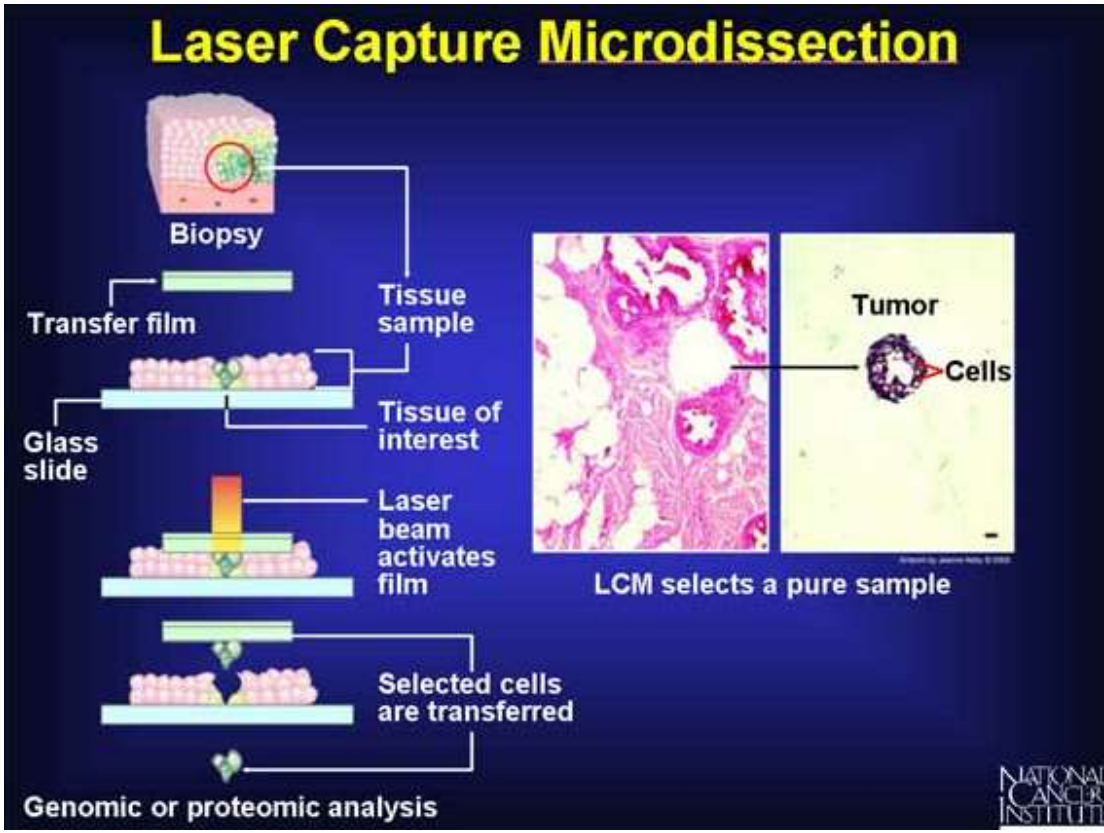

Immune Cell Infiltration
Immune Cell/Dermis Area
0.0004
0.0003
0.0002
0.0001
0.0000
Lesion Border
Normal Region
P1
P2
P3
P4
P5
LCH Patients

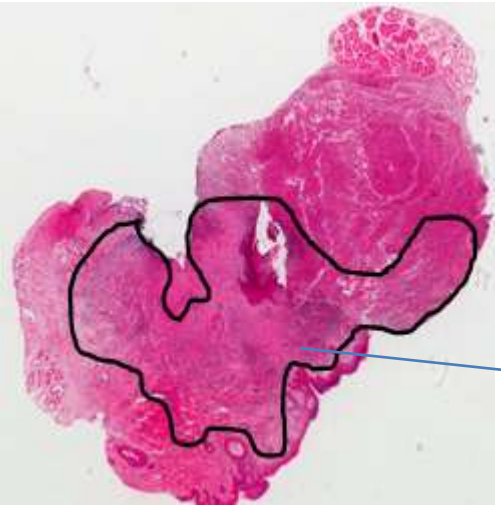

Elastic Fibre Deposition
EF Area/Unit Area
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
Lesion Border
Non-Lesion Region
P1
P2
P3
P4
P5
LCH Patients

3). Gene Expression studies…



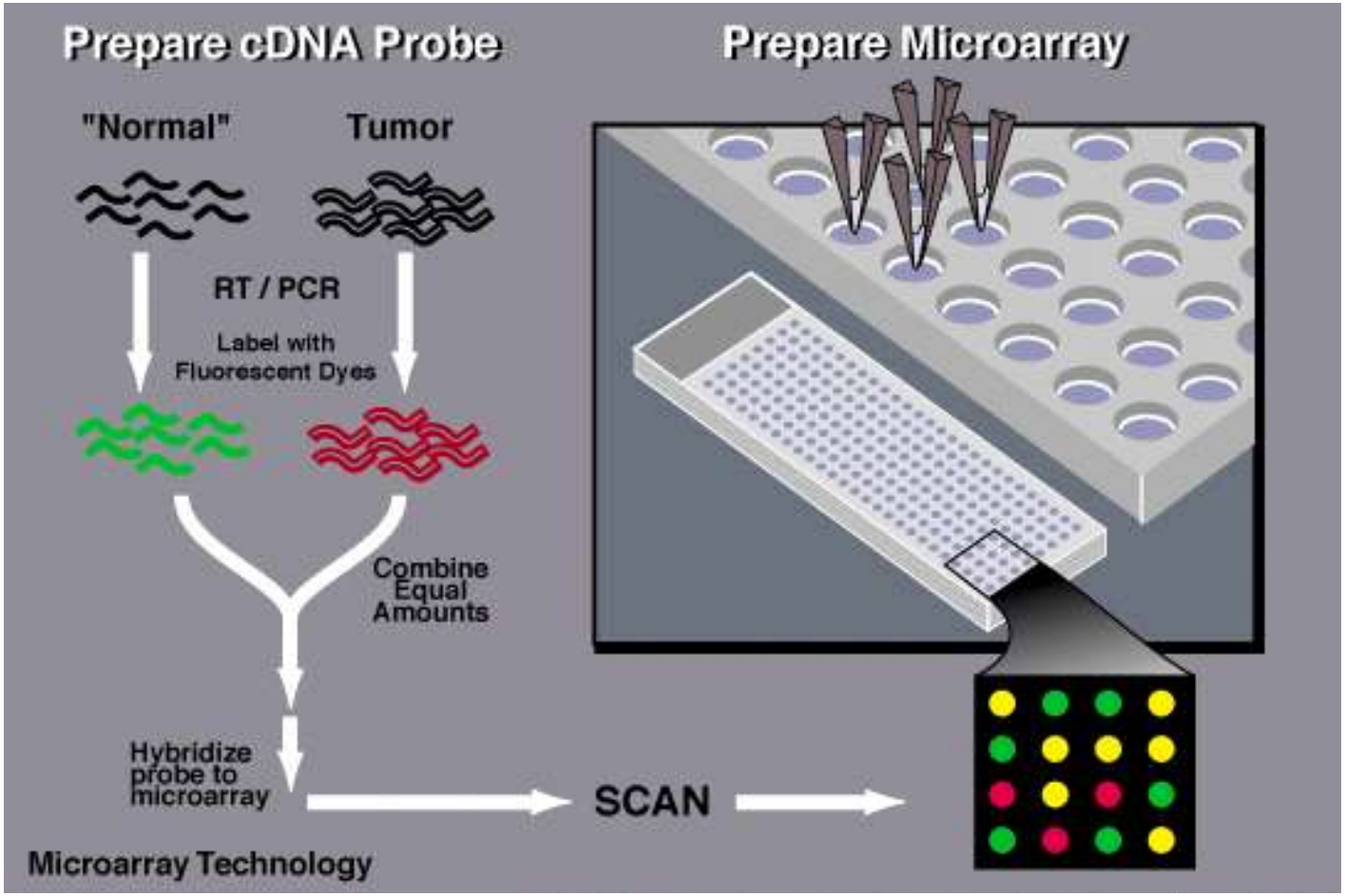
How do we get lesional cells from the biopsy?





Lesional region

Microarrays to Measure Changing Gene Expression




Affymetrix Gene Chip

- Ultimate Goal of Gene Expression Studies:
  - Understand expression level of genes under different conditions

- Helps to:
  - Determines genes involved in a disease
  - Pathways to a disease
  - Use as a screening tool