| Application | Reference | Tissue sample | Techniques used | Potential biomarker |
|---|---|---|---|---|
| Asthma | Wu et al. 2005 | BAL fluid | segmental allergic challenge,SDS-PAGE separation, and nano liquid chromatography-Mass spectrometry(LC-MS/MS) | MMP-9, and its inhibitor TIMP-1 |
| | Cederfur et al. 2012 | BAL fluid | fractionated BAL-fluid samples by galectin affinity chromatography and compared galectin-binding glycoforms by shot-gun proteomics | Proteins only found in asthma patients were macrophage mannose receptor,CD59 and keratin 8.<br>Galectin-8 binding proteins identified only in asthma were haptoglobin, retinoic acid induced G protein-coupled receptor, small breast epithelial mucin, attractin, CD55, alpha-1-acid glycoprotein, CD59 and alpha-1 antitrypsin |
| | O'Neil et al. 2011 | bronchial biopsies | nanoLC-LTQ Orbitrap mass | Seven proteins were significantly different in asthmatic patients compared to controls , including (annexin A5, dermatopontin, histone cluster 1, lamin A/C, peptidylprolyl isomerase A (cyclophilin A), ribosomal protein L7, and ribosomal protein L8) |

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| | Wang et al. 2021 | mouse lung tissue | spectrometery, Ingenuity Pathways Analysis | 20 major clusters of cells were defined as known immune cell types, including four subpopulations of monocytes, ILC2, T-regulators, and basophils among 102 disntinct clusters identified with specific molecular markers |
| COPD | Ohlmeier et al. 2008 | lung tissue and sputum of severe stage IV COPD patients | Two-Dimentional Gel Electrophororsis (2DE) , using Western blotting and immunohistochemistry. | surfactatant protien A (SP-A) |
| | Ohlmeier et al. 2010 | lung tissues from IPF and COPD patients | 2DE, MS, and Western blotting | c-RAGE expression was found to be correlated with COPD progression. |
| | Pastor et al. 2013 | BAL fluid | Extracted proteins were separated using bidimensional polyacrylamide gel electrophoresis (2D-PAGE) and examined by matrix-assisted laser desorption/ionization time of flight mass spectrometry | HSP70 expression was increased in all 3 pathological study groups (COPD, LC, LC/COPD) |

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| Cystic fibrosis | Pollard et al. 2005 | Epithelial lung tissue of cystic fibrosis | de novo biosynthetic labeling<br>2DGE and Mass Spectrometry | identified 20 differentially expressed proteins<br>additional 31 proteins were identified using radiolabeling newly synthesized proteins in CF cells |
|  | Srivastava et al. 2006 | Serum samples from cystic fibrosis patients | antibody capture microarray<br>results were validated by reverse capture protein microarray | 46 proteins were elevated in CF patients compared to controls |
|  | Virginie et al. 2018 | BAL fluid | immunoelectron microscopy, western blotting ,and Mass spectrometry | 4 proteins were found to be increased specifically in CF samples compared to PCD and asthma , which are : Neutrophil gelatinase-associated lipocalin (LCN2), Superoxide dismutase (SOD2), Glutathione peroxidase 3 (GPX3), S100A12 Synaptosomal-associated protein 23 (SNAP23) |

**Table 1 : Applications of precision medicine in pulmonology**

| Reference | Tissue sample | Techniques used | Potential biomarker |
|---|---|---|---|
| Benabdelkamel et. al 2021 | urinary samples | 2D-DIGE with matrix-assisted laser desorption and ionization time of flight (MALDI-TOF) mass spectrometry (MS) | Upregulated proteins in hyperthyroid patients included serotransferrin, transthyretin, serum albumin, ceruloplasmin, and alpha-1B-glycoprotein<br>downregulated urinary proteins were plasma kallikrein, protein glutamine gamma-glutamyl transferase, and serpin B3 (SERPINB3) |

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| Xiao et al. 2021 | Thyroid fluid samples by fine-needle aspiration | Liquid Chromatography–Tandem Mass Spectrometry Analysis<br>Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis | 44 were differenially expressed in HT patients , of which 26 proteins were highly expressed, and 18 proteins being relatively low<br>Several upregulated proteins were found to be related to immune response , such as annexin A6 (ANXA6), calreticulin (CALR), cyclase associated actin cytoskeleton regulatory protein 1 (CAP1). |
| Luo et al. 2018 | serum samples | Ultracentrifugation , Tandem Mass Tag labelling , High performance liquid chromatography (HPLC) analysis, LC-MS/MS, Western blot | 1569 proteins with two or more unique peptides was identified , of which 697 differentially expressed proteins was found in PTC samples of patients with LNM<br>integrin signaling was activated in SPEs of PTC patients with LNM compared to those without LNM |

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| Wei et al. 2023 | cancer tissue and adjacente normal tissue were taken from ten female patients with TNM stage III PTC | TMT labeling and LC/MS/MS | , 147 among 1923 proteins in tumor tissue were considered differentailly expressed proteins in global proteomics, with 78 upregulated proteins and 69 being downregulated<br>57 acetylated proteins were found to be differentially expressed proteins in tumor tissues, including 32 up-regulated and 25 down-regulated ones |
| Z. Li et al. 2022 | Orbital connective tissues from healthy and TAO patients | single-cell RNA sequencing | lipofibroblasts with RASD1 expression were significantly detected in inflammation and adipogenesis associated with TAO |

**Table 2 : Applications of precision medcine in thyroid diseases**.

| Reference | Tissue sample | Techniques used | Potential biomarker |
|---|---|---|---|
| Fischer et al. 2012 | Serum samples | nano LC-MS/MS | Upregulated proteins in AS patients included C-reactive protein (CRP), complement proteins, amyloid P-component serum protein (APCS) and Serpin3A.<br>TF Serotransferrin, SERPINA6 Corticosteroid-binding globulin, and TTR Transthyretin were among the down-regulated proteins |
| S. Liu et al. 2020 | Serum proteins | TMT labeling of peptides, HPLC fractionation, and LC-MS/MS analysis | 46 proteins were upregulated and 56 were downregulated in AS patients compared to healthy subjects<br>C-reactive protein (CRP), complement factor H-related protein 3 (CFHR3), α-1-acid glycoprotein 2 (ORM2), serum amyloid A1 (SAA1), fibrinogen γ (FG-γ), and fibrinogen β (FG-β) were the most significantly upregulated proteins associated with inflammation<br>S100A8, fatty acid binding protein 5 (FABP5), and thrombospondin 1 (THBS1) were the most notably downregulated proteins |

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| Yu et al. 2022 | peripheral blood mononuclear cells (PBMCs) | LC–MS/MS Analysis and validation of Target Proteins Using<br>Parallel Reaction Monitoring | 782 differentially expressed proteins (DEPs) and 122 differentially phosphorylated proteins (DPPs) in AS patients compared to healthy subjects<br>HSP90AA1, HSPA8, ITPR1, MYLK, STIM1,MYL12A, MYL9,and ROCK2 were among the highly expressed proteins. |

**Table 3 : Applications of precision medicine in ankylosing spondylitis.**

| Reference | Tissue sample | Techniques used | Potential biomarker |
|---|---|---|---|
| Salimi et al. 2013 | Skin biopsies of lesional and non-lesional components from atopic dermatitis patients | FACS analysis and cell sorting , ILC2 cell culture, Quantitative RT-PCR, and chemotaxis assay. | Skin-derived ILC2s express the IL-33 receptor ST2, which is up-regulated during activation,<br>and are enriched in lesional skin biopsies from atopic patients<br>IL-25 and IL-33 were found to be  the predominant ILC2-inducing cytokines in a mouse model |
| He et al. 2020 | Lesional and nonlesional skin biopsy specimens of AD patients | Single-cell transcriptome analysis | COL6A5+ COL18A1 + fibroblasts sub-population are unique to AD lesional skin<br>dendritic cell population with expression of CCL19 receptor CCR7 |

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| Penkava et al. 2020 | Blood and synovial fluid of knee joint samples | CyTOF staining and analysis, Mass cytometry, Droplet-based single-cell RNA sequencing, and Plate-based single-cell RNA sequencing. | Memory CD8 T cells were found to be 3-folds expanded in the joints of PsA patients compared to peripheral blood<br>Expanded synovial CD8 T cells were found to express<br>cycling, activation, tissue-homing and tissue residency markers |
| J. Liu et al. 2021 | skin biopsies from psoriatic patients and healthy controls | Single-cell RNA-sequencing | Tc17 subtypes expressing the chemokine CXCL13 |

**Table 4 : Applications of precision medicine in dermatology**

| Reference | Tissue sample | Techniques used | Potential biomarker |
|---|---|---|---|
| Cheng et al. 2010 | Liver tissue from recipients rats of liver allograft | 2-DE and Image Analysis, Spot Cutting and In-Gel Digestion, Western Blot Analysis, and MS/MS analyses | Serotransferrin precursor and Hemopexin precursor |

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| Massoud et al. 2011 | serum samples from patients with acute cellular rejection (ACR) and a control group of liver transplantation patients without ACR | Depletion of Highly Abundant Serum Proteins, Multidimensional Liquid<br>Chromatography–Tandem Mass Spectrometry<br>(LC-MS/MS) Analysis | Most significantly upregulated proteins were Ubiquitin-conjugating enzyme E2, HSP60, and NFAT1<br>Most significantly down-regulated proteins were Human apolipoprotein CI, Nuclear protein, and Zinc alpha-2-glycoprotein |
| Welberry Smith et al. 2013 | Serum samples from ten kidney transplant patients with and without diagnosis of delayed graft function | Immunodepletion using the Multiple Affinity Reagent System 14 column , Label-free mass spectrometry | Serum Aminoacylase-1(ACY-1) was undetectable preoperatively but increased markedly postoperatively, particularly in the DGF group |

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| Hu et al. 2019 | serum samples of kidney transplant patients with and without diagnosis of delayed graft function<br>serum, kidney, and heart samples of mice exposed to renal ischemia/reperfusion (IR) injury | High-throughput assays, real-time qPCR, SDS polyacrylamide gel electrophoretic separation | Plasma Corin level was significantly decreased in recipients with DGF compared with recipients without DGF |
| X. Li et al. 2022 | PBMCs and liver tissue samples from liver transplantation patients and healthy controls | Single-cell RNA sequencing analysis | The proportion of CCR6+ CD4+ T cells increased within liver transplant tissue , in addition to exhausted CTLA4+ CD8+ T cells and proliferating MKI6+ CD8+ T cells being increased significantly<br>LDLR was identified as a novel marker of activated Myeloid-derived suppressor cells (MDSC) to prevent liver transplant rejection |

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| Kong et al. 2022 | PBMCs from cABMR patients and control subjects | Single-cell RNA sequencing analysis | MT-ND6, CXCL8, S100A9, NFKBIA were among the upregulated genes in cABMR group in gamma-sigma T cells, CD8 effector T cells, and CD8 MAI T cells. |

**Table 5 : Applications of precision medicine in transplantation surgery**

| Disease | Name of drug/therapy | Type |
|---|---|---|
| ALS | ● Qalsody (Tofersen) | antisense oligonucleotide |
| Hematological malignancies | ● Kymriah (tisagenlecleucel)<br>● Yescarta (axicabtagene ciloleucel)<br>● Tecartus (brexucabtagene autological)<br>● Breyanzi (lisocabtagene maraleucel) | anti-Cluster of Differentiation (CD)19 CARs |
| | ● Abecma (idecabtagene vicleucel)<br>● Carvykti (ciltacabtagene autoleucel) | target B-cell maturation antigen (BCMA) |
| ADA-SCID | Investigational gene therapy | Lentiviral vector gene therapy |

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| SMA | Zolgensma (Onasemnogene abeparvovec) | adeno-associated viral vector |

**Table (6): gene therapy applications**