The innate Immunity and the Natural Killer Cells as Possible Link Between Obesity and Cancer Breast

Thesis

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List of Abbreviations

ADCC	**:**	Antibody-dependent cellular cytotoxicity
AJCC	**:**	American Joint Committee on Cancer
AP	**:**	Activator protein
AP-1	**:**	Activator protein 1
ATM	**:**	Adipose tissue macrophage.
BC	**:**	Breast cancer
BMI	**:**	Body mass index
BMI	**:**	Body mass index
BRCA1	**:**	Breast cancer gene 1
BRCA2	**:**	Breast cancer gene 2
CAC	**:**	Colitis-associated cancer
CD	**:**	cluster of differentiation
CHD	**:**	Coronary Heart Disease
CML	**:**	Chronic myelogenous leukemia
DAMP	**:**	Damage-associated molecular pattern
DASH	**:**	Dietary Approaches to Stop Hypertension
DASH	**:**	Dietary Approaches to Stop Hypertension
DCIS	**:**	Ductal carcinoma in situ
DCIS	**:**	ductal carcinoma in situ
DCs	**:**	Dendretic cells
DEXA	**:**	Dual X-ray absorptiometry
DEXA	**:**	Dual X-ray absorptiometry
DFS	**:**	Disease free survival
EBV	**:**	Epstein- Barr virus
EGFR	**:**	Epidermal growth factor receptor

EGFR	**:**	epidermal growth factor receptor
ERKs	**:**	Extracellular-signal-regulated kinases
ERT	**:**	Estrogen replacement therapy
ERT	**:**	Estrogen replacement therapy
FNA	**:**	Fine-needle aspiration
G-CSF.	**:**	Granulocyte colony-stimulating factor
GERD	**:**	Gastroesophageal Reflux Disease
GSK-3	**:**	Glycogen synthase kinase 3
GVT	**:**	Graft-versus-tumor
H&E	**:**	hematoloxylin & eosin stains
HLA	**:**	Human leukocyte antigen
HLH	**:**	Hemophagocytosis lymphohistiocytosis
ICAM-1	**:**	Intercellular Adhesion Molecule 1
IDC	**:**	Invasive ductal carcinomas
IDC	**:**	invasive ductal carcinomas
Ig	**:**	immunoglobulin
IGFs	**:**	Insulin-like growth factors
IHC	**:**	Immunohistochemical
IIH	**:**	Intracranial hypertension
IIH	**:**	idiopathic intracranial hypertension
ILC	**:**	Invasive lobular carcinomas
ILC	**:**	Invasive lobular carcinomas
iNKT	**:**	Invariant Natural Killer T
IPAF	**:**	IL-1b-converting enzyme (ICE) protease-activating factor
IRAK4	**:**	IL-1 receptor–associated kinase 4
ITAM	**:**	immunoreceptor tyrosine based activation motif

JAK2	**:**	Janus kinase 2
KIRs	**:**	Human killer cell Ig- like receptor
LAK	**:**	Lymphokine-activated killer
LCIS	**:**	lobular carcinoma in situ
LCIS	**:**	lobular carcinoma in situ
LFA	**:**	Lymphocyte function-associated antigen
LPS	**:**	Lipopolysaccarides
LT	**:**	lymphotoxin
LTβR	**:**	LTβ receptor
MAL	**:**	MyD88 adapter-like
MARK	**:**	Mitogen activated protein kinase
MCP-1	**:**	monocyte chemotactic protein-1
MGL	**:**	Macrophage galactose N-acetyl-galactosamine specific lectin
MHC classI	**:**	Major histocompitability class I
MHO	**:**	Metabolically healthy obese
MIP	**:**	Macrophage inflammatory protein
MM	**:**	Matrix metalloproteinases
MMPs	**:**	Matrix metalloproteinases
mNK	**:**	mature NK
MPL	**:**	Monophosphoryl lipid A
MRD	**:**	minimal residual disease
MyD88	**:**	Myeloid differentiation primary response gene 88
NAFLD	**:**	Nonalcoholic fatty liver disease
NASH	**:**	Nonalcoholic steatohepatitis
NCoR	**:**	Nuclear receptor corepressor
NCRs	**:**	Natural cytotoxicity receptors

NF-κB	**:**	Nuclear factor kappa-light-chain-enhancer of activated B cells
NK	**:**	Natural killer
NKT	**:**	Natural killer T
NLR	**:**	Nucleotide oligomerization domain–like receptor
NLRP3	**:**	NLR family, pyrin domain-containing 3
NOD	**:**	Nucleotide oligomerization domain
OS	**:**	overall survival
PAI-1	**:**	Plasminogen activator inhibitor-1
PAMPs	**:**	pathogen associated molecular patterns
PI3K	**:**	Phosphatidylinositol 3-kinase
PI3K	**:**	Phosphatidylinositol 3-kinases
PI3K	**:**	phosphatidylinositol 3-kinase
PLZF	**:**	transcriptional regulator promyelocytic leukemia zinc finger
pNK	**:**	NK precursor
POMC	**:**	pro-opiomelanocortin
PSGL-1	**:**	P-selectin glycoprotein ligand
RAAS	**:**	Renin-angiotensin aldosterone system
RANTES	**:**	Regulated upon Activation, Normal T-cell Expressed, and Secreted).
RAS	**:**	renin-angiotensin system
RCTs	**:**	Randomized controlled trials
RT-PCR	**:**	Reverse transcriptase-polymerase chain reaction), reverse transcriptase-polymerase chain reaction).
SNP	**:**	Single nucleotide polymorphism

SNS	**:**	Sympathetic nervous system
SPARC	**:**	Scalable Processor Architecture
STAT	**:**	Signal Transducers and Activators of Transcription" protein
SVF	**:**	Stromal vascular fraction
T	**:**	Primary tumor
TCR	**:**	T cell receptor
TF	**:**	transcription factor
Th2	**:**	T-helper lymphocyte type 2
TIR	**:**	Toll/IL-1 receptor–like domain
TIRAP	**:**	Toll/IL-1 receptor–like domain–containing adaptor protein
TLRs	**:**	Toll-like receptors
TNF-α	**:**	Tumor necrosis factor alpha
TNM	**:**	Tumor, nodes, metastases system
UICC	**:**	Union International Contre le Cancer
ULBPs	**:**	UL16 binding protein;
VDUP-1	**:**	Vitamin D3 upregulated protein 1
VEGF	**:**	Vascular endothelial growth factor
VEGF	**:**	Vascular endothelial growth factor
WAT	**:**	White adipose tissue
WHO	**:**	World Health Organization
WHR	**:**	Waist to hip ratio

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Introduction

The prevalence of obesity has increased considerably over the past 20 years because of increased caloric intake and reduced physical activity. It has been estimated that 20% of the world's population is overweight and nearly 300 million are obese (BMI >30 kg/m^2) ***(James et al., 2004).***

Obesity is linked with higher risk of many chronic diseases, including cancer, heart disease, diabetes, hypertension (high blood pressure), kidney disease, stroke, gall bladder disease and sleep disorders ***(James et al.,2004).***

The relationship between obesity and many forms of cancer is well established.

Obesity increases the risk of several solid tumors, including breast, prostate, pancreatic, and colon. One of several mechanisms that may underlie the relationship between obesity and tumor risk is an obesity-induced impairment in immune function; however, little work has been done to examine which components of the immune system are adversely impacted by obesity ***(Rebecca et al., 2007).***

Furthermore, several lines of evidence have supported a link between adipose tissue and immunocompetent cells. This interaction is illustrated in obesity, where excess adiposity and impaired immune function have been described in both humans and genetically obese rodents ***(Egesten et al., 2008).***

However, limited and often controversial information exist comparing immunity in obese and non-obese subjects.