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Manuscript NO: 54361

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MicroRNA sequences modulating inflammation and lipid accumulation in macrophage 'foam' cells: Implications for atherosclerosis

Lightbody RJ *et al.* MicroRNA involved in foam cell formation

Richard James Lightbody, Janice Marie Walsh Taylor, Yvonne Dempsie, Annette Graham

Abstract

Accumulation of macrophage 'foam' cells, laden with cholesterol and cholesteryl ester, within the intima of large arteries, is a hallmark of early 'fatty streak' lesions which can progress to complex, multicellular atheromatous plaques, involving lipoproteins from the bloodstream and cells of the innate and adaptive immune response. Sterol accumulation triggers induction of genes encoding proteins

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Insulin promotes macrophage foam cell formation: Potential ...

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Excessive **lipid accumulation** by **macrophages** plays a crucial role in the initiation and progression of **atherosclerosis**. **Lipid** laden **macrophage foam cells** accumulate in atheromatous plaque and promote **inflammation** by secreting cytokines that recruit other immune **cells** to the arterial intima.

Cited by: 25

Author: Young M Park, Young M Park, Sangeeta R ...

Publish Year: 2012

MicroRNA-33–dependent regulation of macrophage metabolism ...

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4665799

Dec 01, 2015 · **Macrophages** are critical **effectors of inflammation** and innate immunity; they also regulate adaptive immunity by recruiting and/or activating other **immune cells** at **inflammatory foci** (1). In addition, **macrophages** **play** important roles in **tissue homeostasis** and resolution of **inflammation** (2).

Cited by: 185

Author: Mireille Ouimet, Hasini N. Ediriweera, U. Ma...

Publish Year: 2015

Inhibition of microRNA-17-5p reduces the inflammation and ...

https://www.sciencedirect.com/science/article/pii/S1347861318302172

Furthermore, **cellular cholesterol** **accumulates** in **lipid-engorged macrophage foam cells**, leading to **lipid deposition** at the core of atherosclerosis. 12 Thus, inhibiting the **lipid accumulation** is an important therapeutic strategy for AS. **Cholesterol efflux** is the main pathway for **reducing lipid accumulation in macrophages**.

Cited by: 1

Author: Lili Tan, Limin Liu, Zhenyu Jiang, Xiaoqiao H...

Publish Year: 2019

MicroRNA Regulation of Atherosclerosis | Circulation Research

https://www.ahajournals.org/doi/full/10.1161/circresaha.115.306300

On differentiation into **macrophages**, these **cells** play central roles in the pathophysiology of atherosclerosis by **maintaining lipid homeostasis** in the vessel wall and **secreting inflammation-promoting** mediators that act on both immune and **nonimmune cell** types in the artery wall. 91 Lipoprotein uptake by **macrophages** in the nascent plaque results in the formation of **lipid-laden macrophage foam cells** ...

Cited by: 244

Author: Mark W. Feinberg, Kathryn J. Moore

Publish Year: 2016

Macrophages in atherosclerosis: a dynamic balance | Nature ...

https://www.nature.com/articles/nri3520

Sep 02, 2013 · Abstract. Atherosclerosis is a **chronic inflammatory disease** that arises from an **imbalance in lipid metabolism** and a maladaptive immune response driven by the **accumulation of cholesterol-laden macrophages** in the **artery wall**. Through the analysis of the progression and regression of atherosclerosis in animal models,...

Cited by: 1302

Author: Kathryn J. Moore, Frederick J. Sheedy, Edw...

Publish Year: 2013

Inflammation and its resolution in atherosclerosis ...

https://www.nature.com/articles/s41569-019-0169-2

Mar 07, 2019 · Modified **lipoproteins** and **cholesterol crystals** **accumulate** in the arterial intima and **induce foam cell formation** and **inflammation**. Defective efferocytosis of **apoptotic foam cells** leads to necrotic core formation. Defective efferocytosis is a sign of failure in the resolution of **inflammation**.

Cited by: 67

Author: Magnus Bäck, Arif Yurdagul, Ira Tabas, Kat...

Publish Year: 2019

Author: Magnus Bäck

Cytokines, macrophage lipid metabolism and foam cells ...

https://www.sciencedirect.com/science/article/pii/S0163782711000191

Other **macrophage** actions during the disease include the production of chemokines and the secretion of ECM-degrading proteases. **Macrophages** also undergo apoptosis, particularly in advanced atherosclerotic lesions where free cholesterol **accumulation in foam cells** triggers apoptotic signals such as the ER stress-UPR-CHOP pathway.

Cited by: 283

Author: James Edward McLaren, Daryn Robert Mic...

Publish Year: 2011

Mechanisms of foam cell formation in atherosclerosis ...

https://link.springer.com/article/10.1007/s00109-017-1575-8

Aug 07, 2017 · Elevated expression of LOX-1 leads to **increased lipid uptake** by **macrophages**. By contrast, expression of ABCA1 and ABCG1 is decreased in atherosclerosis, further aggravating **intracellular cholesterol accumulation** and promoting **generation foam cells formation** [13].

Cited by: 106

Author: Dimitry A. Chistiakov, Alexandra A. Melnich...

Publish Year: 2017

microRNA-33 Regulates Macrophage Autophagy in Atherosclerosis

https://www.researchgate.net/publication/316315496...

Macrophage-specific loss of miR-33 decreases lipid accumulation and **inflammation** under **hyperlipidemic conditions**, leading to reduced **plaque burden**.

MicroRNA-33–dependent regulation of macrophage metabolism ...

https://www.jci.org/articles/view/81676

In **atherosclerosis**, where **macrophages** are key integrators of **inflammatory** and metabolic signals that drive plaque progression, metabolic reprogramming by anti-miR-33 promoted the **accumulation** of M2 **macrophages** and FOXP3 + Tregs in plaques, decreased markers of systemic **inflammation**, and reduced plaque size. Importantly, we found that miR-33 ...

MicroRNA sequences modulating inflammation and lipid accumu



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Macrophages in atherosclerosis: a dynamic balance

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Turning to apoptosis, the continued presence of **macrophage foam cells** in the **inflammatory**, **lipid-rich** environment of the plaque can eventually lead to cytotoxicity from ER and oxidative stress

1. Activation of ER stress responses occurs as a result of **free cholesterol accumulation in macrophages** and by saturated fatty acids signaling via SRA, TLR2 and TLR4 75 .

Cited by: 1302

Author: Kathryn J. Moore, Frederick J. Sheedy, ...

Publish Year: 2013

MicroRNA-33–dependent regulation of macrophage metabolism ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4665799>

Dec 01, 2015 · Introduction. **Macrophages** are critical effectors of **inflammation** and innate immunity; they also regulate adaptive immunity by recruiting and/or activating other immune **cells** at **inflammatory** foci (). In addition, **macrophages** play important roles in tissue homeostasis and resolution of **inflammation** (). To fulfill these functions, **macrophages** can adopt a spectrum of ...

Cited by: 185

Author: Mireille Ouimet, Hasini N. Ediriweera, U....

Publish Year: 2015

Macrophage miRNAs in atherosclerosis - ScienceDirect

<https://www.sciencedirect.com/science/article/pii/S1388198116300270>

The interaction between **cholesterol accumulation** and **inflammatory activation** means that therapeutic targeting of **macrophage foam cells** will ultimately **reduce inflammation** in the vessel wall and thus reduce atherosclerotic lesion burden.

Cited by: 10

Author: Denuja Karunakaran, Katey J. Rayner

Publish Year: 2016

microRNA-33 Regulates Macrophage Autophagy in Atherosclerosis

<https://www.ahajournals.org/doi/full/10.1161/atvbaha.116.308916>

In **atherosclerosis**, **lipid-laden macrophage foam cells** accumulate in the artery wall, where they



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Macrophages in atherosclerosis: a dynamic balance

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357520>

Turning to apoptosis, the continued presence of **macrophage foam cells** in the **inflammatory, lipid-rich** environment of the plaque can eventually lead to cytotoxicity from ER and oxidative stress 1. Activation of ER stress responses occurs as a result of **free cholesterol accumulation in macrophages** and by saturated fatty acids signaling via SRA, TLR2 and TLR4 75 .

Cited by: 1302 **Author:** Kathryn J. Moore, Frederick J. Sheedy, E...

Publish Year: 2013

MicroRNA-33–dependent regulation of macrophage metabolism ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4665799>

Dec 01, 2015 · In the setting of hypercholesterolemia, monocyte-derived **macrophages** infiltrate the arterial intima to clear retained apolipoprotein B–containing (apoB-containing) lipoproteins (**e.g., LDL**) and are transformed into **lipid-laden macrophage foam cells** . For reasons that are poorly understood, these **macrophage foam cells** persist in the artery wall, setting off a maladaptive immune response that ...

Cited by: 185 **Author:** Mireille Ouimet, Hasini N. Ediriweera, U. ...

Publish Year: 2015

MicroRNA-27 Prevents Atherosclerosis by Suppressing ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4892477>

It is well known that the development of atherosclerosis, a chronic vascular disease, is closely associated with the **subendothelial accumulation of macrophages** and derived **foam cells**[33–36], one of the hallmarks of atherosclerosis. High expression of **pro-inflammatory cytokines** and **excessive accumulation of lipids** in **activated macrophages** have been shown to promote the progression of ...

Cited by: 29 **Author:** Wei Xie, Liang Li, Min Zhang, Hai-Peng C...

Publish Year: 2016

MicroRNA-mediated mechanisms of the cellular stress ...

<https://www.nature.com/articles/nrcardio.2015.38>