

QUERY THIS: M2 MACROPHAGES

SCIENCE PERFECTED IN MARKET®



Chronic Lung Inflammation, BerriQi® and Macrophages

With long term exposure to allergens such as pollution, urban dust or foreign particles, our lungs may suffer from chronic inflammation. With chronically inflamed lungs, our airways fill with mucus, and the delicate tissues surrounding our airways are swollen with infiltrating immune cells, serum fluid and serum proteins. Our lung tissues suffer damage from destructive enzymes and reactive oxygen species released by the infiltrating immune cells, and become scarred by abnormal collagen fibre deposition in a process called tissue remodelling.

Daily BerriQi® consumption, concurrent with ongoing allergen exposure in preclinical models of chronic airway allergic inflammation, resulted in cleared airways, lower numbers of immune cell infiltrates in the lungs, a reduction in tissue swelling, removal of the abnormally deposited collagen fibres, and strengthening of the walls of the major airways, all clearly demonstrated by lung histology. BerriQi prevents the abnormal tissue remodelling by working through M2 macrophages.

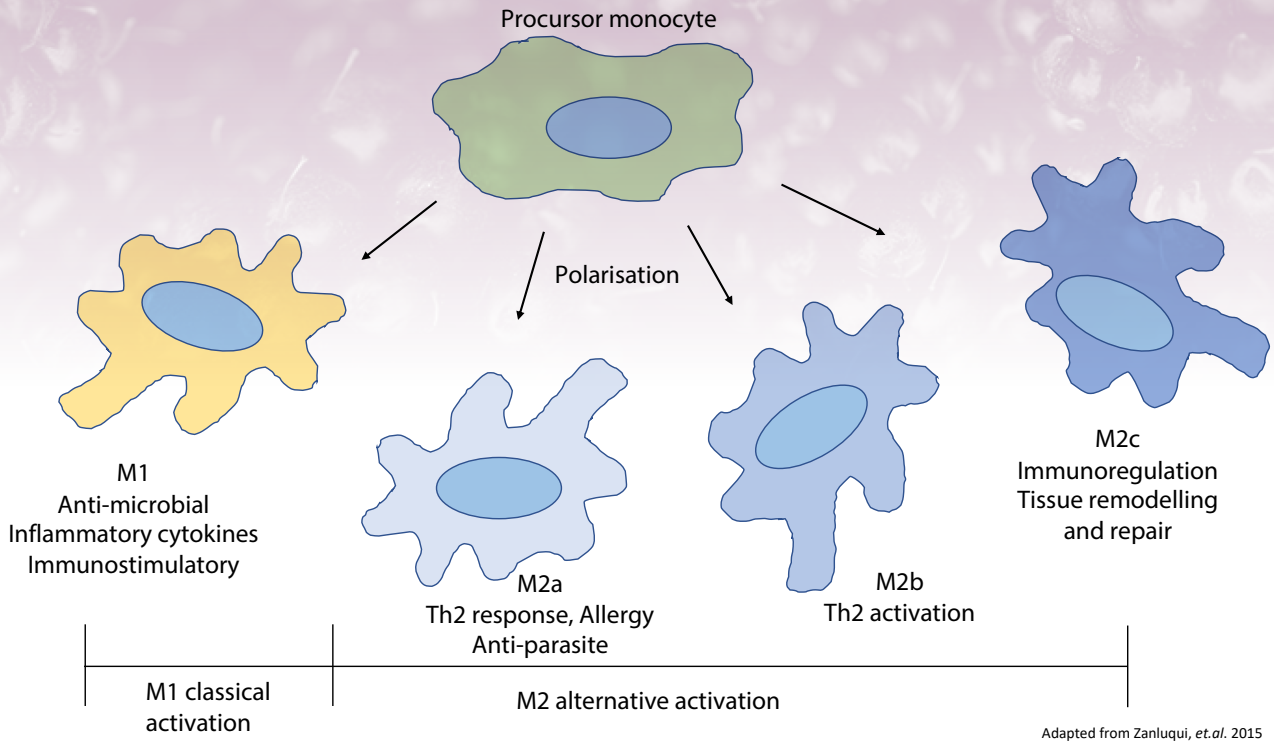
What Are Macrophages?

Macrophages are a type of immune cell which patrol our tissues and organs for foreign/invading particles or our own dead tissue to consume through a process called phagocytosis. Phagocytosis involves surrounding and engulfing the target and then destroying it within the macrophage. Because of this process macrophages are also called phagocytes. In addition to patrolling and phagocytosing, macrophages signal and recruit other cells of the immune system to the site of activity. This signalling and recruiting happens by the macrophages releasing cytokines and chemokines. These are protein or chemical messengers which stimulate other immune cells - including more macrophages - to migrate to the site of invasion or injury. Finally, macrophages release protein-degrading protease enzymes and reactive oxygen species to remodel tissue and destroy invading cells. These three processes, phagocytosis, immune signalling and releasing destructive compounds, makes macrophages essential components in infection and wound defence and repair.

However, during uncontrolled, persistent, chronic inflammation, fibrotic macrophages may cause significant scarring and collateral damage to the surrounding tissues. The activation of the M2 wound-repair mode of macrophages is important to resolve this.

What Does M2 Mean?

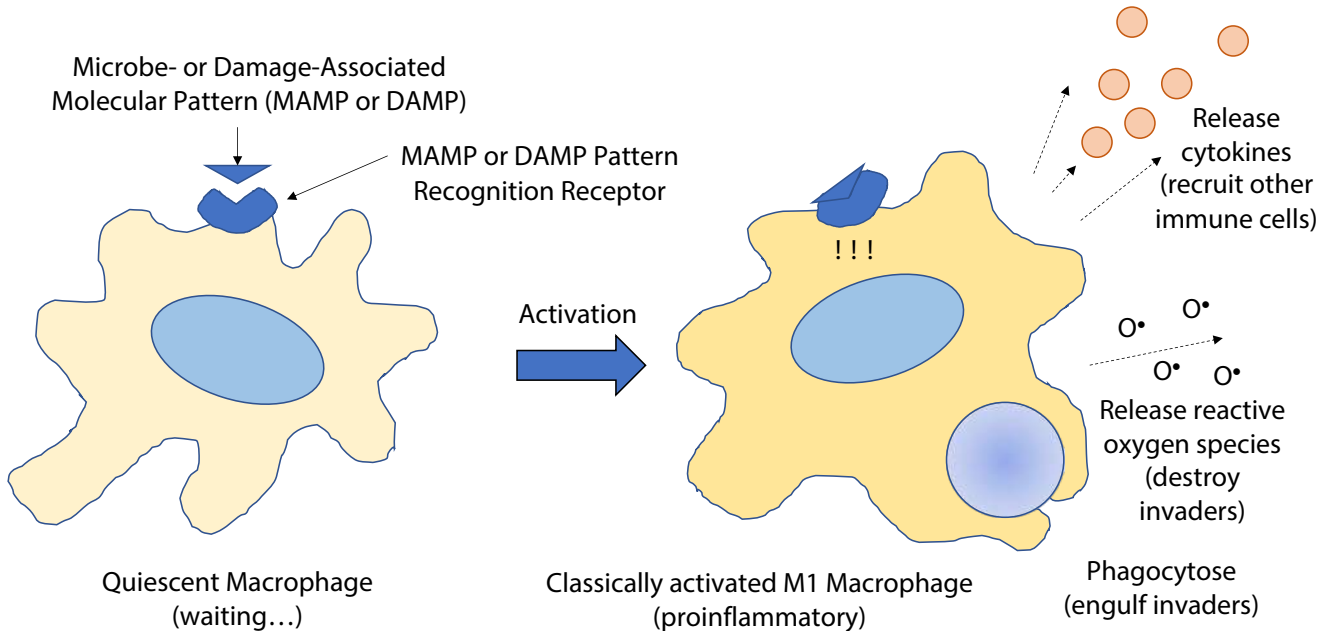
M2 designates that the macrophages are of the alternatively activated sort, which happens in the post-inflammatory repair phase of an infection or injury. Because of this, M2 macrophages are sometimes called alternatively activated macrophages. This is in contrast to the M1, classically activated macrophages, which happen as an early response to infection or injury. The conversion of a macrophage from the M1 to M2 type is called class switching. However, class switching is not an abrupt "on/off" conversion. Instead, macrophages function on a spectrum which corresponds to the status of the site of infection or injury.



Wound Repair and Classes of Macrophages

Acute tissue injury causes cell death and release of what are known as damage-associated molecular patterns (DAMPs). In a non-sterile environment such as skin, additional microbe-associated molecular patterns (MAMPs) may also be present. Collectively these DAMPs and MAMPs are recognised by

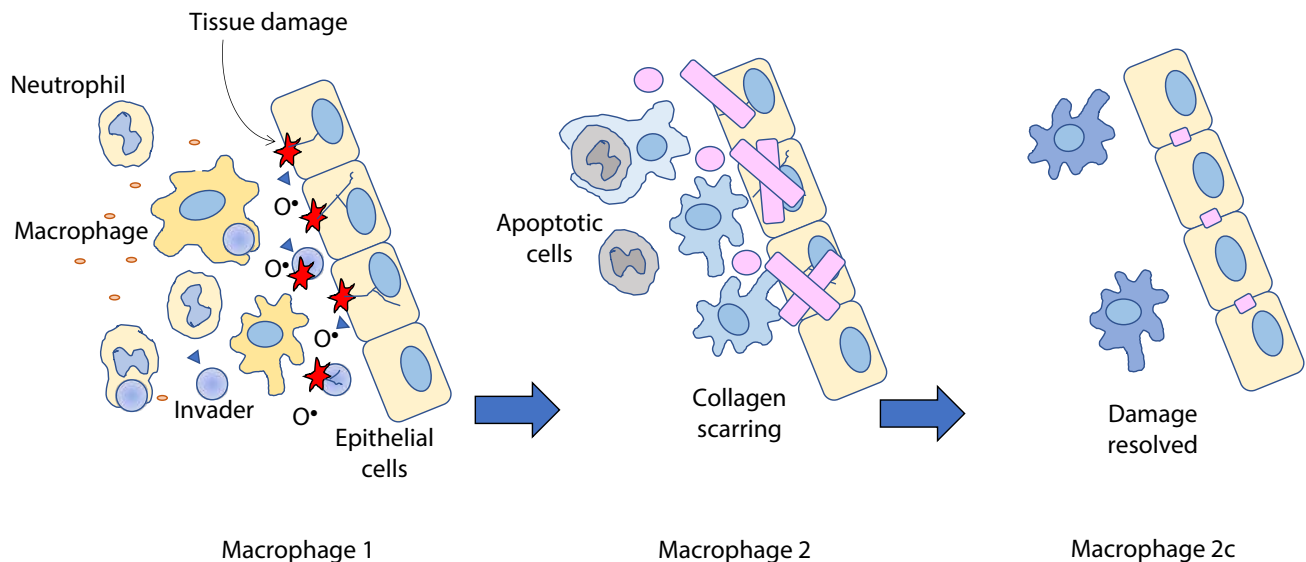
pattern recognition receptors (PRR) on the surface of resident tissue macrophages and some other immune cells. PRRs stimulate the macrophages to switch on a pro-inflammatory state. This is known as classical activation.



Macrophages and other recruited immune cells, such as neutrophils and eosinophils, then clear away damaged tissue and any invading microorganisms. This process can be lifesaving but may result in substantial collateral tissue damage.

After the source of DAMPs and MAMPs is removed, the other infiltrating immune cells die off in a process of programmed cell death called apoptosis. Apoptotic cells signal the

macrophages to switch to an anti-inflammatory state, which send further anti-inflammatory signals, and promote tissue regeneration. However, inappropriate collagen may be deposited by fibrotic macrophages and other cells called fibroblasts. Ultimately this will result in scar tissue devoid of protein messengers or chemical messengers, which signals macrophages to enter a fibrolytic, collagen-degrading fully M2 phase.



All of these types of macrophages can coexist in different micro-areas of the same tissue, with regions of active, acute inflammation, early wound repair, late wound repair, scar formation and scar removal.

It is in our best interests to resolve chronic lung inflammation and the associated collateral tissue damage and scarring by having our macrophages in the M2 state.

What Can I Do About My Macrophages?

Based on our preclinical studies, we suggest that our recommended bioactive daily dose of 7.4 g BerriQi juice concentrate may support normal post-inflammatory wound repair responses by encouraging the class-switching of macrophages to a fibrolytic M2 macrophage which help to reduce lung scarring.



For more information, please contact:

Email: info@anagenix.com
 Tel: +64 9 520 0831
www.anagenix.com

