

Available online at www.sciencedirect.com

ScienceDirect

Biomedical Journal

journal homepage: www.elsevier.com/locate/bj

Highlights

Microbes are off the menu: Defective macrophage phagocytosis in COPD

Emma Louise Walton*

Staff Writer at the Biomedical Journal, 56 Dronningens gate, 7012 Trondheim, Norway

ARTICLE INFO

Article history:

Available online 1 February 2018

Keywords:

Macrophages

Phagocytosis

COPD

Diagnostic bacteriology

Automation

ABSTRACT

In this issue of the Biomedical Journal, we learn about the pathophysiology of chronic obstructive pulmonary disease and how defective macrophage phagocytosis may lead to the build up of microbes and pollutants in inflamed lungs. We also focus on new findings that may take us a step closer to full automation in diagnostic bacteriology laboratories. Finally, we highlight the anti-tumor properties of microalgae and the application of algorithms to predict human emotion from electrocardiogram.

Spotlight on review

Microbes are off the menu: defective macrophage phagocytosis in COPD

Chronic obstructive pulmonary disease (COPD) is a chronic and progressive family of diseases including emphysema and chronic bronchitis characterized by vicious inflammation and destruction of the lung parenchyma [1]. The exact cause of COPD is unclear, but under conditions of COPD, resident lung macrophages appear to fail in their duties to clean up pollutants, pathogens as well as dying cells and other debris, and it is thought that this defect contributes to the pathogenesis of the disease. In this issue of the *Biomedical Journal*, Jubrail et al. [2] describe the important role of phagocytosis in lung immunity and bring us up-to-date with the latest research on macrophages in COPD.

The human lungs are a major interface between the body and the environment and as such, have the difficult challenge of maintaining homeostasis when faced with environmental insults like pollutants and pathogens. Policing this space is a wide array of immune cells, including three distinct populations of lung macrophages. Their main job is to clear inhaled particulate matter and pathogens through phagocytosis, whereby macrophages ingest and digest this foreign material. This results not only in the clearance of the material but also in antigen presentation and cytokine production and hence a coordinated immune response.

In light of its importance in lung immune responses, it comes as no surprise that phagocytosis is perturbed in COPD. It is, in part, an environmentally-induced disease, with long term exposure to pollutants like cigarette smoke putting individuals at risk of developing COPD [3]. Although the chronic inflammation in COPD causes an increase macrophages in the lung parenchyma [Fig. 1], their phagocytic function is

* Corresponding author.

E-mail address: ewalton86@gmail.com.

Peer review under responsibility of Chang Gung University.

<https://doi.org/10.1016/j.bj.2017.12.002>

2319-4170/© 2018 Chang Gung University. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

impaired [4]. This defect appears to be more pronounced with certain substrates, with one study finding that alveolar macrophages from COPD patients showed impaired phagocytosis towards Non Typeable *Haemophilus influenzae*, a common respiratory pathogen associated with exacerbations of the disease [5]. Whether smoking exacerbates this defect is currently the subject of some debate, with some studies finding no link [6], others finding more pronounced defects only in active smokers with the disease [7].

Given the link between defective macrophage phagocytosis and COPD various new treatment ideas are being explored to restore the defects in this disease. Various organic and non organic compounds have shown promise at restoring macrophage phagocytic and inflammatory responses in vitro, in vivo and in certain patient cohorts and the results now need further characterisation to prove their potential future utility in COPD.

Thus, phagocytic dysfunction very much appears to be a hallmark of COPD and indeed other respiratory diseases [8], but we still know far too little about the nature of the defect. Such work could lead to the design of intelligent therapies to limit disease progression or prevent exacerbations.

Spotlight on original article

A step towards full automation in diagnostic bacteriology

Ever since the first automated instrument, the Autoanalyzer I, was introduced in 1957 [9], automation has been steadily replacing manual work in all fields of laboratory medicine. Diagnostic bacteriology, however, had been lagging behind other fields somewhat due to the complexity of specimen types and analytical processes. In this issue of the *Biomedical Journal*, Croxatto et al. [10] take the field one step further

towards full automation by providing proof-of-concept that intelligent algorithms can accurately detect, semi-quantify and identify bacteria in clinical specimens.

Over the past decade, increasing automation in bacterial diagnostics has enabled laboratories to keep up with increased demand on ever limited budgets. Several automated specimen processors are available on the market to enable inoculation, incubation, plate management and digital imaging, and the use of such technology has increased productivity and quality, while reducing time to results [11,12]. Yet a truly fully automated system should be able to perform the subsequent follow-up work, which today is still largely confined to human hands, namely identifying the bacterial species and its antibiotic susceptibility. The development intelligent image analysis algorithms to identify bacteria may one day enable reliable results to be delivered without any human intervention.

In this context, Croxatto et al. set out to develop algorithms to detect, identify and quantify bacterial colonies using a training set of known strains and a testing set of clinical urine samples. Each sample was inoculated of three different types of media and was imaged every 2 h from 0 to 24 h after inoculation using a BD Kiestra™ system. A group of technicians visually inspected each plate to detect, count and identify bacteria, and the exact strain was determined through matrix-assisted laser desorption ionization. To develop the image analysis algorithm, random forest classifiers were used to distinguish microbial from non-microbial objects, semi-quantify bacteria and identify them based on morphology, color and overall phenotype.

Compared to human visual inspection, which was considered “the final truth”, the detection algorithm showed a sensitivity of 97.1% and a specificity of 93.6%. Bacteria were quantified with an accuracy of 80%, even though there were multiple species growing in some of the clinical samples.

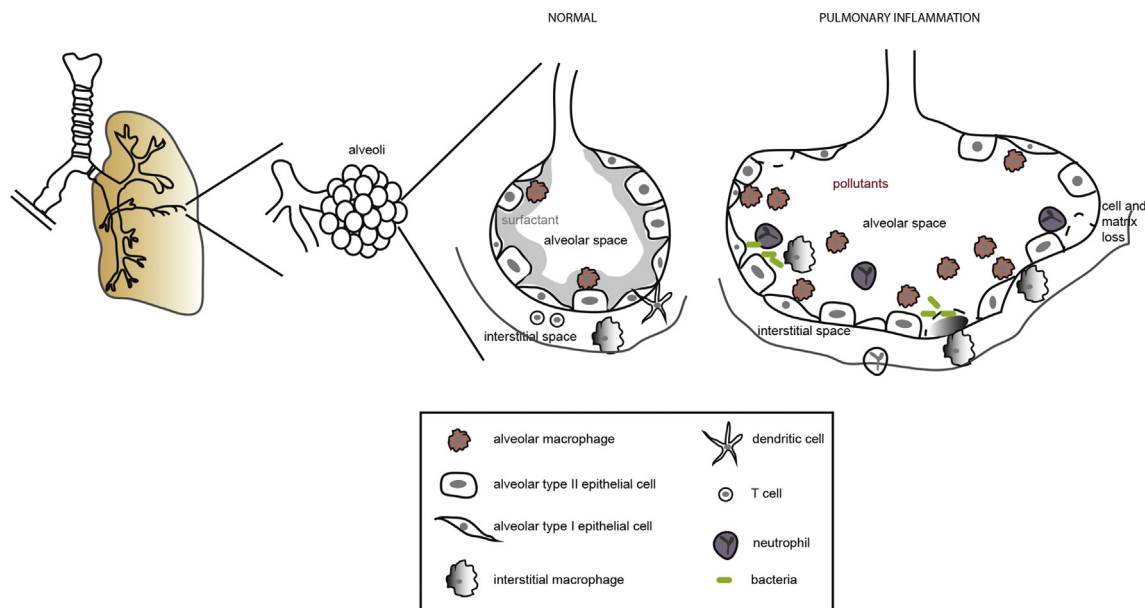


Fig. 1 Lung immune cell populations under steady state and inflammatory conditions. Chronic exposure to pollutants causes inflammation, leading to an increase in macrophages and other immune cells. Figure kindly provided by Jubrail et al. [2].

Depending on the species, the algorithm identified the bacterial colonies with an accuracy of 93–98%, and even outperformed human inspection for one of the three types of culture media used.

These findings highlight the potential of automated analysis to improve laboratory workflow in the setting of diagnostic bacteriology. Clearly, such models require further validation and refinement, in particular taking into account the specific media plates used for bacterial growth, which affected the results of Croxatto's study [10]. But algorithms with built in flexibility allowing users to adapt them to specific in house conditions may facilitate and speed up analysis in both in diagnostic bacteriology and other settings, like screening for positivity in normally sterile samples.

Also in this issue

Short review

Gasdermins: a new family of cell death inducers

In this short review, Ramos-Junior and Morandini [13] describe the emerging role of gasdermin D during pore formation in the highly inflammatory, lytic form of cell death called pyroptosis.

Original articles

Image fusion for neurosurgical planning

When assessing brain injuries and planning for surgery, computed tomography (CT) and magnetic resonance imaging (MRI) are two indispensable imaging modalities offering complementary information. A CT scan provides a detailed evaluation of cortical bone and can detect fractures quickly, whereas MRI offers high soft tissue contrast and can reveal small or subtle lesions. However, the two images are collected independently and combined retrospectively in a process that is often error-prone. Nandish et al. [14] test approaches to fuse CT and MRI images. Their findings could be applied to improve neurosurgical planning.

Fighting tumor cell growth with microalgae

Plants and microorganisms have proven to be excellent sources of compounds for chemotherapy. Extracts of microalgae, a water-dwelling unicellular organism, inhibit cancer cell growth both *in vitro* and *in vivo*, without affected healthy cells [15]. Jabeen et al. [16] apply different purification processes to liberate MA proteins and test the ability of the resulting extracts to inhibit the growth of well-known human cancer cell lines. Their findings identify MA constituents as a promising starting point for the pharmaceutical development of anti-cancer formulations.

Safety and efficacy of an anti-epileptic drug in Taiwanese patients

Most people with epilepsy suffer from seizures that can be controlled (with varying degrees of success) through anti-epileptic drugs. One of the newest anti-epileptics, the AMPA glutamate receptor antagonist, perampanel, was shown to be effective at controlling seizures as an adjunct therapy in three

randomized controlled trials [17–19]. It was approved in Taiwan in 2015, but there is a lack of real-world data on the use of the drug in Asian patients. In this retrospective analysis of 210 patients with epilepsy, Chiang et al. [20] find that with around 50% of patients responding to treatment, the efficacy of perampanel is similar to that observed in other ethnic groups. Their findings however warn that patients with pre-existing psychiatric conditions and taking perampanel require special monitoring.

Reading emotions through algorithms

The development of algorithms capable of automatically recognizing human emotion has many applications, ranging from psychology and mental health to computer–human interactions like gaming. Here, Goshvarpour et al. [21] recorded electrocardiograms and galvanic skin responses of healthy students listening to emotional music and successfully apply matching pursuit algorithms to the data to classify emotional responses.

Conflict of interests

The author declares no conflict of interests.

REFERENCES

- [1] <http://www.who.int/respiratory/copd/en/> [Accessed 20 December 2017].
- [2] Jubrail J, Kurian N, Niedergang F. Macrophage phagocytosis cracking the defect code in COPD. *Biomed J* 2017;40:305–12.
- [3] Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007;370:765–73.
- [4] Hodge S, Hodge G, Scicchitano R, Reynolds PN, Holmes M. Alveolar macrophages from subjects with chronic obstructive pulmonary disease are deficient in their ability to phagocytose apoptotic airway epithelial cells. *Immunol Cell Biol* 2003;81:289–96.
- [5] Berenson CS, Garlipp MA, Grove LJ, Maloney J, Sethi S. Impaired phagocytosis of nontypeable *Haemophilus influenzae* by human alveolar macrophages in chronic obstructive pulmonary disease. *J Infect Dis* 2006;194:1375–84.
- [6] Berenson CS, Kruzel RL, Eberhardt E, Sethi S. Phagocytic dysfunction of human alveolar macrophages and severity of chronic obstructive pulmonary disease. *J Infect Dis* 2013;208:2036–45.
- [7] Hodge S, Hodge G, Ahern J, Jersmann H, Holmes M, Reynolds PN. Smoking alters alveolar macrophage recognition and phagocytic ability: implications in chronic obstructive pulmonary disease. *Am J Respir Cell Mol Biol* 2007;37:748–55.
- [8] Donnelly LE, Barnes PJ. Defective phagocytosis in airways disease. *Chest* 2012;141:1055–62.
- [9] <https://www.mlo-online.com/the-power-of-laboratory-automation.php> [Accessed 18 December 2017].
- [10] Croxatto A, Marcelpoil R, Orny C, Morel D, Prod'homme G, Greub G. Towards automated detection, semi-quantification and identification of microbial growth in clinical bacteriology: a proof of concept. *Biomed J* 2017;40:317–28.
- [11] Dauwalder O, Landrieu L, Laurent F, de Montclos M, Vandenesch F, Lina G. Does bacteriology laboratory automation reduce time to results and increase quality management? *Clin Microbiol Infect* 2016;22:236–43.

- [12] Croxatto A, Prod'hom G, Faverjon F, Rochais Y, Greub G. Laboratory automation in clinical bacteriology: what system to choose? *Clin Microbiol Infect* 2016;22:217–35.
- [13] Ramos-Junior ES, Morandini AC. Gasdermin: a new player to the inflammasome game. *Biomed J* 2017;40:313–6.
- [14] Nandish S, Gopalakrishna P, Rajagopal KV. Multiresolution image registration for multimodal brain images and fusion for better neurosurgical planning. *Biomed J* 2017;40:329–38.
- [15] Talero E, Garcia-Maurino S, Avila-Roman J, RodriguezLuna A, Alcaide A, Motilva V. Bioactive compounds isolated from microalgae in chronic inflammation and cancer. *Mar Drugs* 2015;13:6152–209.
- [16] Jabeen A, Reeder B, Hisaindee S, Ashraf S, Darmaki NA, Al-Zuhair S, et al. Effect of Enzymatic pre-treatment of microalgae extracts on their anti-tumor activity. *Biomed J* 2017;40:339–46.
- [17] French JA, Krauss GL, Biton V, Squillacote D, Yang H, Laurenza A, et al. Adjunctive perampanel for refractory partial-onset seizures: randomized phase III study 304. *Neurology* 2012;79:589–96.
- [18] French JA, Krauss GL, Steinhoff BJ, Squillacote D, Yang H, Kumar D, et al. Evaluation of adjunctive perampanel in patients with refractory partial-onset seizures: results of randomized global phase III study 305. *Epilepsia* 2013;54:117–25.
- [19] Krauss GL, Serratosa JM, Villanueva V, Endziniene M, Hong Z, French J, et al. Randomized phase III study 306: adjunctive perampanel for refractory partial-onset seizures. *Neurology* 2012;78:1408–15.
- [20] Chiang HI, Lim SN, Hsieh HY, Cheng MY, Chang CW, Wu T. Preliminary Asian experience of using perampanel in clinical practice. *Biomed J* 2017;40:347–54.
- [21] Goshvarpour A, Abbasi A, Goshvarpour A. An accurate emotion recognition system using ECG and GSR signals and matching pursuit method. *Biomed J* 2017;40:355–68.