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The Development of New Antimicrobial Pathways: Combatting the Threat of Antimicrobial Resistance

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Abstract

This report is in extension of that presented in International Journal of Sciences: Basic and Applied Research (IJSBAR) by the current researcher (author) in respect of “site attachment inhibition (or, negation of cellular attachment by viruses)” as a new pathway for development of antiviral drugs (therapies) given the lack of success by the two pathways established to date which have focused on "virus replication" and "immune system enhancement." In that research report, the new antiviral treatment pathway was clearly delineated and supported in a number of ways including the example of HIV with CCR5-Δ32 mutation creating innate resistance (or, immunity) by way of subsequent site attachment inhibition, in addition to other blockade support. This report presents the conceptualization of “site attachment inhibition of bacteria (or, negation of cellular attachment by bacteria)” as a new pathway in antimicrobial treatment, in addition to consideration of other potential pathways. The pathway appears viable, although not appearing as robust at this stage as that for antiviral therapy. The author of the current report has been invited to present the new strategic pathway delineated, specifically site attachment inhibition (or, negation of cellular attachment by infective agents), at the 6th International Conference on Immunology (USA; Chicago IL 870th Congress) and related presentations of the official International Conference Series Umbrella including Rome, Italy.

Keywords: Antimicrobial; Bacteria; CCR5-Δ32; Covalent Bonds; Electromagnetic Radiation; Glycoprotein; Microorganism; Resistance.

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1. Introduction

The concern with respect to antimicrobial resistance and the associated health threat has gained increasing attention. There has been difficulty in gaining traction with respect to the issue and, given the lack of success, ongoing attention directed toward the issue is required [1-4].

This report is in extension of that presented in IJSBAR by the current researcher in respect of "site attachment inhibition (or, negation of cellular attachment by viruses)" as a new pathway for development of antiviral drugs (therapies) given the lack of success by the two pathways established to date which have focused on: virus replication; and, immune system enhancement" [4-7]. In that research report, the new antiviral treatment pathway was clearly delineated and supported in a number of ways including the example of HIV with CCR5-Δ32 mutation creating innate resistance (or, immunity) by way of the subsequent site attachment inhibition, in addition to blockade and antagonism support [8-9].

The current report explores the potential for analogous development in respect of bacterial infection. That is, the conceptualization of site attachment inhibition (or, negation of cellular attachment by bacteria) as a new pathway for antimicrobial treatment.

2. Attachment of Bacteria to Cells

Bacteria attach to human cells through a bacterial adhesin to form bonds (including covalent bonds) with the human cells. Bacteria sometimes reside on the surface of human cells but can also enter the cells. At this stage, there are two key fundamentals to take from this [10]:

1. The attachment by bacteria to glycoprotein receptors
2. The attachment mechanism through adhesins and formation of covalent bonds

The report will, therefore, continue by way of consideration with respect to the above two key fundamentals as the systematic process for pathway development.

3. Bacterial Attachment: Glycoprotein Receptor Attachment

Common receptors for attachment by bacteria to human cells are glycoprotein receptors. This would suggest a possible approach to site attachment inhibition (negation of cellular attachment by bacteria) may be represented by "glycoprotein receptor antagonism" or "glycoprotein receptor blockade." In considering the potential support for success of this strategy:

(1)Treatment of specific blood disorders (requiring negation of platelet aggregation and thrombus formation) utilize a class of drugs (medications) termed Glycoprotein IIb/IIIa inhibitors [6], and it seems reasonable to suggest that inhibition, antagonism, or blockade of other glycoprotein receptors, in addition to any other receptors of relevance, would be worth considering seriously as a potential pathway for treatment of bacterial

infections.

(2) The human immune system attempts to coat infective agents (bacteria, viruses and the like) as a means to negate attachment by bacteria (and other infective agents) to the human cells [11], and therefore it makes scientific sense to pursue this new pathway for antibacterial development.

Although the scientific support (evidence) for this pathway with respect to bacteria is not as robust as that for site attachment inhibition of viruses, presented in the previous report published in IJSBAR, taking into account increasing threats posed by resistant bacteria globally, the pathway impresses as worthy of pursuit.

4. The attachment through adhesins and covalent bonds

Bacteria commonly form bonds when attaching to human cells through adhesins and covalent bonds, whether the category of bacteria is of that which resides on the surface of human cells or of a category that enters human cells. It is therefore worth considering, as a further method for site attachment inhibition (negation of cellular attachment by bacteria) the pathway represented by breaking adhesins and covalent bonds.

The pathway at this stage would be exploratory and would likely (for each type of bacteria) involve the exploration of:

1. Electromagnetic radiation that may break (or, destroy) the given adhesins and covalent bonds
2. Chemicals that may break (or, destroy) the given adhesins and covalent bonds
3. Other vibrating waveforms, temperatures, and agents that may break (or, destroy) the given adhesins and covalent bonds

In considering the potential support for success of this strategy there has been a degree of research to demonstrate that perhaps radiation can kill infective organisms including bacteria [12,13].

5. Areas for further research:

Further research may be directed toward other infective agents including fungi, parasites and other relevant agents. In addition, the mechanisms above (e.g. electromagnetic radiation and other) may be explored in respect of their ability to directly kill (destruct) the given infective agents of interest, in addition to the strategic method of site attachment inhibition (negation of cellular attachment by bacteria). Other axes of combat with regards to negation of cellular attachment by infective agents should be explored. For instance, gene therapy to target disruption of the DNA of the given infective agent (example, bacteria) from forming the apparatus used in attachment to the human cells. At present, gene therapy in combating infectious diseases essentially focuses on disrupting the cellular replication of the given infective agent.

With respect to the previous publication in IJSBAR, and not wanting to depart too far from the topic at hand, it may also be worth investigating measures including knockout of genes in the prenatal (or, earlier) stages of

development as a means to prevent cancer, for instance the knockout of proto-oncogenes.

One further area to explore may be with respect to the merger of technology and biology. The merger of technology and biology has become increasingly evident with examples being attempts at three dimensional printing of human organs and the use of analogous reasoning as supportive data in process development of new strategic antimicrobial pathways. There are also predicted developments in areas, at a minimum, revolving around: downloadable consciousness; and, technological mapping of the human CNS [14,15]. It may be an option to explore, given the increasing trend for merging biology and technology, whether infective agents can be integrated into advanced computing, or quantum, analytical systems in order to derive solutions, for instance a destructive waveform or vibration. In further support of the above, other literature also espouses biological infective agents as similar to information technology infective agents (or, viruses) and it would not seem likely that resources would be wasted in exploration of methods to analyze IT equivalents of the given infective agents in order to derive a solution able to be converted back to a biologically applicable form [1,16].

The above being said, it should be stated that advances in such areas as downloadable consciousness and the merging of biology with technology raises definite ethical considerations that should be considered by society and ethics committees. The author of the current report has assessed in a previous report the possibility of even viruses containing some degree of consciousness (or, at least an ability to sense surroundings) [1].

Whilst the above may seem some way down the track, the prospect may be nearer than first impressions may suggest given the mind mapping goals set by the Brain Initiative program commenced in America [15].

6. Summary

The previous report in IJSBAR by the current researcher identified significant issues: A) The lack of successful antiviral drugs (therapies) despite many years of pursuit; B) No cure for HIV despite many years of exploration. The pathways to combat HIV and other viruses to date: 1) virus replication; 2) enhancement of immune function. Furthermore, given the lack of success achieved by these two pathways, that it would seem reasonable to direct focus at development of a new strategic pathway. The research report presented the development of the new strategic pathway for antiviral therapies represented by site attachment inhibition (or, negation of cellular attachment by viruses). Further to this, HIV was used in case analysis with strategic measures detailed including prenatal genetic therapy focusing on mutagenesis and knockout, targeted at genes (receptors; and, surface proteins) including CCR5 and CXCR4, as a means of achieving innate resistance (immunity) similar to the known CCR5-Δ32 mutation, in addition to treatment strategy following established infection designed to block attachment of the virus to CCR5 and CXCR4, including antagonism and blockade of the receptors (analogous to beta blockade), stem cell therapy, radiation, and targeted therapy designed to attack the mechanisms of the virus in its attachment ability to the given receptors (CCR5, CXCR4) and any other relevant. Support for site attachment inhibition strategy was further consolidated through consideration with respect to advanced information technology in which one key mechanism for virus removal is represented by negation of site attachment.

The current report has presented, in extension of the aforementioned research, the development and conceptualization of site attachment inhibition of bacteria (or, negation of cellular attachment by bacteria). At this stage, there are two key fundamentals to take from this:

1. The attachment by bacteria to glycoprotein receptors
2. The attachment mechanism through adhesins and formation of covalent bonds

In considering the potential support for success of this strategy:

(1) Treatment of specific blood disorders (requiring negation of platelet aggregation and thrombus formation) utilize a class of drugs (medications) termed Glycoprotein IIb/IIIa inhibitors [6], and it seems reasonable to suggest that inhibition, blockade or antagonism of other glycoprotein receptors would be worth pursuing as a potential pathway for treatment of bacterial infections.

(2) The human immune system attempts to coat infective agents (bacteria, viruses and the like) as a means to negate attachment by bacteria (and other infective agents) to the human cells [11], and therefore it makes scientific sense to pursue this new pathway for antibacterial development.

This pathway regarding site attachment inhibition (i.e. for bacteria) may not be as robust at this stage as that for viruses presented in the previous report however, given the current global context of antibiotic resistance, would definitely seem worth pursuing.

Based on the evidence, including the innate immunity (resistance) achieved by CCR5-Δ32 mutation, it seems optimistic that there is potential for site attachment inhibition to be a successful therapeutic modality by itself in respect of viruses without requiring polypharmacy or adjunctive treatments. It is not entirely clear whether in respect of bacteria the likelihood of site attachment inhibition being a successful modality purely by itself is perhaps lower due to the enhanced ability of bacteria to survive in conditions of site attachment negation given the reduced (or lack of) reliance, relative to viruses, on the internal machinery of human cells.

7. Conclusion

This report presents the development and conceptualization of *site attachment inhibition of bacteria (or, negation of cellular attachment by bacteria)* as a new pathway in antimicrobial therapeutics, in addition to consideration of other potential pathways.

The pathway appears viable, although not appearing as robust at this stage as that for antiviral therapy presented previously by the current researcher in IJSBAR. That being said, particularly given the current context of antibiotic resistance, it seems reasonable to suggest the pathway as worth pursuing.

In conclusion, the research presented by the author of the current and previous reports has developed and conceptualized the new strategic pathway for combatting infective agents represented by *site attachment*

inhibition (or, negation of cellular attachment by infective agents). This is particularly important in the current global context of antibiotic resistance and deficiencies in effective antiviral drugs (therapies).

The researcher of the current report has been invited to present the new strategic pathway delineated, specifically site attachment inhibition (or, negation of cellular attachment by infective agents), at the 6th International Conference on Immunology (USA; Chicago IL 870th Congress) and related presentations of the official International Conference Series Umbrella including Rome, Italy. .

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Biographical Notes

Simon Raymond is a Consultant (medicine and surgery) specialising in Medical and Scientific Research and an Alumnus of Melbourne University (Rank of Number 1 in Australia and Number 33 in the World). The above stated Researcher has acted as a Reviewer for the respected Medical Journal of Australia, has received invitations internationally to review from prestigious medical journals including Journal of American Medical Association Network. He has received award in recognition of his research by Royal Australasian College of Surgeons (PSC, 2006) and invited to conferences internationally as an official Delegate and Researcher, including that in USA and China. Dr Simon Raymond is a graduate of medical school who shifted from clinical practitioner medicine and surgery into a focus on high level scientific research. Dr Simon Raymond has acted as the Principle Researcher in the highest-powered form of medical trial—Randomised Controlled Trial (RCT). The above stated Researcher is also a Member of the Golden Key International Society for Honoured and outstanding Academics and has been cited as a Notable Global Leader. Dr Simon Raymond's research has been indexed by well respected universities including Cornell University.