INNATE IMMUNITY: FROM FLIES TO HUMANS

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Insects make up nearly 80% of all extant species on earth and present a formidable challenge : they put one third of humanity at continuous risk of often severe diseases, namely through their role as vectors of various types of pathogens. Although insects have long been known to be strongly resistant to infections, the mechanisms underlying this resistance, other than the well known process of phagocytosis, have only been addressed relatively recently.
A general picture of these defences has now evolved and Drosophila is to be largely credited for this progress. Flies, like all invertebrates, rely solely on innate immunity for their antimicrobial defenses. Remarkably, the unravelling of the Drosophila antimicrobial defences has had a significant impact on understanding essential facets of mammalian innate immunity.
The presentation will briefly review the major developments in the study of host defences in flies over the last two decades. Emphasis will be put on the identification of effector polypeptides and on the control of expression of the corresponding genes, on the recognition mechanisms of infecting agents and the the subsequent activation of intracellular signalling cascades by these receptors. This progress will be put in parallel to that of studies performed in various laboratories on mammalian immune defences and on similar reactions in other phyla. An evolutionary scheme will be proposed for innate immune defenses.
Further reading :
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USING LABORATORY SCIENCE TO INDIVIDUALISE CARE IN DIABETES

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Using laboratory Science to Individualise care in Diabetes
In many diseases laboratory science is central in defining subtypes of disease that require different treatment. Traditionally this has not been the case in diabetes where the major subgroups Type 1 and Type 2 diabetes are recognised clinically. The recent advances in molecular genetics has shown that there are specific monogenic forms of diabetes that require specific treatment and hence making a correct diagnosis is critical and requires advanced laboratory science
There is clear heterogeneity in the familial form of diabetes known as Maturity-onset diabetes of the young and these have different treatment requirements.. Patients with hepatic nuclear factor-1alpha (HNF1A) mutations have progressive beta-cell deterioration and require treatment. HNF1A patients are 4 times more sensitive to sulphonylureas than matched type 2 diabetic patients. Patients with a glucose-sensing beta-cell defect due to glucokinase mutations have regulated, mild, fasting hyperglycaemia. Oral hypoglycaemic agents or low-dose insulin have no impact on glycaemic control. HNF1beta is expressed in pancreatic stem cells before differentiation into endocrine or exocrine cells, so patients with HNF1beta mutations have reduced pancreatic development, resulting in early-onset diabetes and exocrine dysfunction. These patients usually rapidly require insulin.
Half patients diagnosed with neonatal diabetes before 6 months have a mutation in the KATP channel. The mutated KATP channel in these patients does not close in response to increased ATP concentrations, but can be closed when sulphonylureas bind to the sulphonylurea receptor 1 subunit of the channel. These patients are insulin dependent, but have excellent glycaemic control on high-dose sulphonylureas tablets.
In conclusion, the defining of molecular genetic aetiology in monogenic diabetes has identified several specific beta-cell defects, and these are critical in determining the response to treatment. This means laboratory science is now critical in the diagnosis of subtypes of diabetes.

MOLECULAR MEDICINE REVOLUTION – ITS IMPACT IN THE CLINICAL LABORATORY

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During the five past decades, the advances in clinical laboratories are astonishing with a lot of great breakthroughs and I am convinced that we are only at the beginning of the story. These progresses have been made possible thanks to parallel unbelievable advances in fundamental biology knowledge and outstanding technological developments. Automation had been the main source of progress in clinical laboratories during the 70' – 90' and the present robots are able to do almost everything from a blood sample to a result pre-interpreted by expert systems. There is an enormous technological gap between these systems and the prehistorical Technicon AutoAnalyser invented by Leonard Skeggs in 1957, leading to a considerably increased medical benefit for the patients.
The real medical progress has come from advances in fundamental biology knowledge and the development of new high throughput and/or very high sensitivity instruments. A typical example is mass spectrometry. It is now possible do determine the molecular mass of any molecules, including proteins, with a precision of less than 1 Da, from a genuine patient sample. I am sure that 20 years ago nobody could imagine that a mass spectrometer would become an absolute must for a microbiologist, as it allows the characterization of bacteria in few minutes with a cost divided by ten.
Hyper sensitive systems allowing analysis at the level of a single cell or a single molecule are used in research laboratories and those dedicated to clinical diagnosis are under development. The development of New Generation Sequencing (NGS), which allow the determination of a DNA sequence of up to 300 Gb in a single run represents a true revolution and the systems are already used in many clinical laboratories.
With the development of high throughput multiplex analyses: NGS, DNA chips, Lab-on-a-chip… and the fundamental biological data obtained thanks to the various "Omics" as proteomics, genomics, transcriptomics, metabolomics… studies, thousands of biomarkers should be discovered. They are the basis of the new types of Biology and Medicine that are on the way. They are called system biology and personalized (now also called precision) medicine. The Biologist will play a major and central role in these new approaches.