Disease in Plant and Animal: Similarities and Differences

Firoozeh Chamandoosti

Iranian Research Institute of Plant Protection, Agricultural Research, Education and Extension Organization (AREEO), Tehran, Iran
PhD of Cellular and Developmental Biology, Assistant Professor of Iranian Research Institute of Plant Protection Department of Plant Diseases

Abstract— *According to current human opinion and knowledge living organisms can be divided into seven kingdoms. The similarities and differences between these seven groups also the relationships between them are very interesting. These relationships lead to creation the different kinds of biological terms such as, mutualism, commensalism and parasitism. So plants and animal also microorganisms have to fight sometimes. The mechanisms of pathogenicity and the mechanisms of defense can be either similar or different. Emphasizing aspect of pathogenicity of some microorganisms, such as Salmonella, Fusarium and Tobacco mosaic virus can case to disease in plants and animals.*

Keywords— Animal diseases, Defense system, Plant diseases, Pathogenicity.

I. INTRODUCTION

Our enormous universe contains of wonderful diversity of living organisms. More than of strange of wonderful diversity, the relationships between this living things is very interesting and surprising. Briefly these relationships divide to profitable and detrimental. For example the all of relations between plants, animal and humans with harmful microorganisms are detrimental. In the same way that living things are very different, they have a lot of common characteristics. Alike these differences and similarities between living things, also their relationships have similar characteristics and dissimilar characteristics. For example we can consider relation between host plants and animal plants with their specific pathogens. The manner of combat for plants and animals against their pathogen based on their cellular characteristics either host cell or pathogen cell is different. In fact because of the marked differences between their cellular structures and modes of life, it is not unreasonable to expect that very different strategies for attack, defense, and counterattack would have evolved in plants and animals against their respective pathogens [1].

The ability of pathogenic microorganisms to harm both animal and plant hosts has been documented since the initial demonstration in the 1870s that microbes were causal agents of disease. Since the initial discoveries by [2] that *Bacillus anthracis* caused anthrax and by [3] that *Erwinia amylovora* caused fire blight in pears, our knowledge base has expanded enormously.

In this paper we try to point the mechanisms of pathogenicity in plants and animals, defense systems in plants and animals against their pathogens and finally parallels in pathogenesis on plant and animal hosts

II. THE MECHANISMS OF PATHOGENICITY IN PLANTS AND ANIMALS

The first step in the recognition of a pathogen is a general response, when non – specific receptors on the surface of plant or animal cells detect non – specific PAMPs (pathogen – associated molecular patterns). These molecules regularly occur in bacteria, fungi and in several other microbes. Typical examples are: lipo polysaccharides, peptidoglycans, chitin, and bacterial flagella. PAMP – receptors can be regarded as multi domain proteins with similar biological functions and protein structures [4; 5; 6; 7; and 8]. When these plant or animal receptors are activated by PAMPs, general reactions are stimulated in infected hosts. Ion fluxes are activated, an oxidative burst is initiated, and mitogen – activated protein kinases (MAP kinases) are expressed.

Furthermore, a set of transcriptional changes occur, in plants, so – called pathogenesis – related proteins and phytoalexins are being accumulated. All these alterations may have roles in PAMP – induced immunity (pattern –triggered immunity) [9and 7]. Although PAMP – triggered immunity can be considered as a general response of plant or animal organisms to pathogens, another type of immunity permits the inhibition of specific pathogenic races in resistant hosts. In these cases specific effectors of pathogenic races trigger the immune response [10]. In both plants and animals, a lipid compound, phosphatidyl – inositol 3 – phosphate mediates entry of pathogen effectors into host cells [11]. Plant or animal NLR receptor (Nucleotide – binding domain and Leucine – rich Repeat – c containing receptors) that interact with these effectors possess a very specific recognition ability. Interestingly, effector recognition by a receptor is associated with an almost infinite number of effector

(antigen) –binding ability of animal receptors. In this case somatic recombination and mutation is generated in the receptor – carrying lymphocytes determining a high degree of immune diversity. Effector recognition by a receptor results in clonal expansion of lymphocytes and formation of memory cells having receptors with effector – binding specificity identical to that of lymphocytes. These procedures allow a secondary immune response against a subsequent infection.

An adaptive immune system does not exist in plants. Plants have no lymphocytes, immune memory cells are not formed and the phenomenon of somatic recombination has not been unequivocally demonstrated. However, as regards similarity, plant NLR Receptors, the r – proteins also have nucleotide – binding and leucine – rich – repeat domains like their animal counterparts. In addition, there is a secondary immune response operating in plants that confers inhibition of secondary infections and is triggered by a primary infection that occurred earlier in a distal plant organ. This phenomenon is called systemic acquired resistance (SAR) [12; 13; and 14].

One can raise the question, how can plants develop specific resistance mechanisms induced by numerous effectors of different pathogenic races? Plants do not have an adaptive immune system that is the basis of immune diversity in animals. Only a limited number of specific receptors (r – proteins) exist in plant organisms, and still, immune plants can recognize a high number of effectors of pathogenic races. The "gene – for – gene concept" tried to answer this question [15]. According to the original experiments rust – resistant flax strains express different r – genes corresponding to specific avirulence (effector) genes in each pathogenic rust race. In each incompatible (resistant) host/pathogen combination an avirulence gene encodes a specific effector and a plant r – gene encodes a specific receptor. Thus, an effector of a race can activate only the corresponding specific plant receptor. However, it turned out that only a few hundred r – genes exist in host plants, as compared to the almost infinite number of effectors encoded by pathogen avirulence genes. Therefore, this concept cannot explain the high degree of immune capacity and broad immune diversity of plants.

Recent investigations on the mechanism of plant non – adaptive immunity point to the possibility that plants may exhibit a different type of immune diversity. Several results have shown that plant r – protein receptors do not directly recognize effectors of pathogens as foreign proteins in most host/pathogen combinations. Rather, pathogen effectors modify target self – proteins in plants in the course of the infection process As a result of the photolytic activity, phosphorylation, acetylation etc. exerted by effectors, the modified self – proteins become "foreign" (non – self) for plant receptors. Thus, the receptor r – protein can recognize the modified target self – protein. This is the essence of the "guard hypothesis". An r – protein is somehow connected to a target self – protein(s). After modifications, target proteins are able to initiate recognition processes and an immune response develops [16; 17; and 18].

It seems clear from the "guard hypothesis" that only a limited number of receptor r –proteins will be required to recognize different pathogenic races because the very large number of effectors released by those races may modify the same target protein. It also turned out that a large number of effectors can alter only a few conserved target self – proteins, which will be able to activate r – proteins. Thus, immunity will be initiated in a very large number of plant cultivar/pathogenic race combinations. It would seem that immune diversity may exist also in plants, because only a small number of r – proteins can recognize an almost infinite number of races – specific effectors.

As a consequence of the effector receptor interaction signal transduction chains are activated and, in the end, invading pathogens will be inhibited or killed. A series of genes are activated or inhibited in the resistant plant. However, the role of these genes in the immunity process is not exactly clear so far [19]. Surprisingly demonstrated that similar gene groups are activated in infected hosts whether the plant exhibits susceptibility or resistance. In the case of compatible or incompatible *Arabidopsis–Pseudomonas* combinations one can detect common mRNA expression profiles. If we compare specific and non – specific immune processes, again same or similar gene groups are activated [20 and 21]. All these facts refer to the possibility that timing of gene activations, Rather than gene alteration itself has a pivotal role in disease resistance. It was shown in several experiments that those genes are activated much earlier in resistant plants than in susceptible ones. Accordingly it seems reasonable to suppose that different forms of plant immunity have a common basic mechanism.

If an effector protein of a pathogen, modifies a plant protein which has no role in non – self – recognition, this modified protein will not be foreign, therefore will not be recognized by receptor r – proteins.

In this case the pathogen effector acts as a virulence factor rather than an avirulence gene product. In fact, the original function of pathogen effectors is to promote pathogenesis as virulence factors [22]. Therefore, effector proteins of a given pathogen could be regarded as "double agents", as was expressed by [23], since effectors may behave as avirulence factors in

immune processes or virulence factors in reactions of susceptibility. [24] It has been shown that according to the damage or danger signal model in the mammalian immune system the recognition of the modified self – mechanism also exists.

This section is closed with a brief noticing to immunity system in animal especially in invertebrate.

Mobile immune cells and a circulatory system permit diseased animals to exert immunity in the whole body. In addition, immune memory cells are also formed having receptors with antigen – binding ability allowing a secondary immune response to a subsequent infection. This immune memory – based response is a very effective type of adaptive immune response in animals. Interestingly, immune memory operates also in invertebrate animals although they do not have an adaptive immune response system. The mechanism is not well understood at the moment [25].

III. DEFENSE SYSTEMS IN PLANTS AND ANIMALS AGAINST THEIR PATHOGENS

3.1 The kingdoms of life

Charles Darwin described the evolution of species as 'the tree of life, an expression implying that all life originates from a single common root [26]. Until the 1960s, only three kingdoms of life were recognized: the single – celled protista, and the multicellular plantae and animalia. In 1959, Whittaker [27] defined a five domain system distinguishing prokaryotic and eukaryotic single – celled organisms and, in addition, adding fungi as a recognized kingdom [27]. The resulting of five kingdom system became a widely accepted standard. Since then, additional kingdoms have been proposed, of which only two are more or less commonly accepted. Based on rRNA gene differences, a division of prokaryotes into eubacteria and archaea was proposed [28 and29]. In addition, the kingdom Chromista, containing many algal groups as well as most water moulds, was put forward [30]. As a consequence, the generally recognized seven kingdoms of life are as follows.

3.1.1 Kingdom Eubacteria

These unicellular organisms are prokaryotic and lack a nucleus and other membrane – bounded organelles. The cell wall is composed partially of peptidoglycan, a complex structural molecule that is not found in eukaryotic cells.

3.1.2 Kingdom Archaea

Many archaeans are anaerobic and thrive under extreme conditions. Together with the eubacteria they compose the prokaryotes. With respect to cellular structure and metabolism, they resemble eubacteria, while with respect to transcription and translation, they are similar to eukaryotes. In contrast to eubacteria, archaea lack peptidoglycans in their cell wall. This kingdom is not universally recognized, and some systematicians classify archaea as an infrakingdom of the bacteria [31].

3.1.3 Kingdom Protista

This kingdom contains single celled eukaryotes. Protista are unicellular or colonial homokaryotic organisms that can be either autotrophic or heterotrophic. Locomotion occurs by means of flagella or pseudopodia.

3.1.4 Kingdom Chromista

Almost all of the species of the Chromista are photosynthetic, except for the water moulds, and most are also aquatic. Almost all fall into the traditional category of 'algae'. The photosynthetic members possess chlorophyll c, which does not occur in plants or the related 'green algae' (Chlorophyta, Charophyta, etc.). The best – known colourless members of the Chromista are a group with fungus like morphology, the oomycetes.

3.1.5 Kingdom Fungi

These are heterotrophic eukaryotes relatively closely related to animalia but distinguished in part by the possession of cells with acarbohydrate cell wall. Reproduction is usually by means of nonmotile spores or, in one phylum, flagellated zoospores. Somatic structures often appear filamentous and branched, growing only at the apex. Unicellular organisms reproducing by budding are also characteristic of certain groups. Many but not all fungi reproduce sexually as well as asexually. They include moulds, mushrooms, yeasts, mildews, smuts, and rumen symbionts, as well as the conspicuous component of lichens (a symbiosis between fungi and algae or cyanobacteria).

3.1.6 Kingdom Plantae

These are autotrophic, mostly multicellular organisms, usually with haplo – diploid life cycles. They typically develop from embryos and use chlorophyll to convert CO2 with the aid of sunlight into complex carbohydrates.

3.1.7 Kingdom Animalia

This kingdom encompasses heterotrophic multi – cellular organisms whose cells do not synthesise cell walls or photosynthetic pigments. They develop from a diploid blastula. Within these seven kingdoms of life, five major groups of microbial pathogens are currently recognized: bacteria,fungi, protozoa, helminths and oomycetes. Protozoa (kingdom Protista) are single – celled eukaryotes that include amoeba (for instance the Entamoeb species that cause gastrointestinal disease) and a large diversity of other microorganisms (for example the malaria parasites *Plasmodium* spp. and the flagellated Trypanosoma spp.). Helminths (kingdom Animalia) are multicellular invertebrates that, unlike protozoa, have differentiated tissues. Various types of vermiform animals, such as the nematodes that cause elephantiasis and river blindness, are included in this category. Finally, oomycetes (kingdom Chromista) are filamentous aquatic organisms that have cell walls composed of cellulose and a predominantly diploid lifecycle. Asexual reproduction is by biflagellated zoospores. The most well known oomycete pathogen is *Phytophthora infestans*, causal agent of potato late blight that caused the Great Irish Famine (1845 – 1847), when up to one million people died and a similar number emigrated, many to the USA. So far, archaea are not identified as direct causal agents of infectious diseases. However, recent studies show a correlation between infections and the presence of archaea [32]. Therefore it is expected that archaea will be identified as causes of infectious diseases.

3.2 Plant and animal defense

The plant and animal host kingdoms have both innate and inducible/adaptive defense responses that are very different. These defense systems are generally effective in that the majority of fungi in the environment cannot cause disease. The immune system of mammals involves the innate complement system, circulating cells such as phagocytes that can internalize and destroy pathogen cells, and adaptive antibody – mediated defenses. The complement pathway, involving soluble factors and corresponding receptors, can lead to the formation of a pore complex in accessible pathogen membranes and subsequent lysis and opsonization, whereby proteins form a coating on antigens, pathogen cells, or host cells infected by the pathogen. This process "tags" them for clearance by the immune system and can trigger proinflammatory stimulation of chemotaxis [33 and 34].

Many serious fungal infections of mammals occur in immunocompromised hosts, suggesting that mammalian defense systems are usually very effective against fungi. The severity of fungal diseases ranges from serious infections (histoplasmosis, blastomycosis, and coccidioidomycosis) [35] requiring hospitalization to superficial cutaneous infections (e.g., tinea) which are extremely common and caused by fungi such as *Candida* and *Trichophyton* spp.

In contrast, animals' fungal pathogens of plants have developed many mechanisms to evade or overcome healthy host plant defenses. Although plants do not have circulating or phagocytic cells, their cells have a thick, complex wall that acts as a barrier to invasion. Plants display innate pathogen – specific resistance, genetically controlled via resistance genes. Additionally, plants display inducible systemic acquired resistance, which occurs when previous exposure to a pathogen activates signaling pathways acting via molecules such as jasmonate, ethylene, and salicylic acid. These small and sometimes volatile molecules spread throughout the plant or even the plant population. This triggers responses such as the expression of "pathogenesis related proteins," including chitinases or glucanases, which can lead to the increased resistance of the whole plant against a subsequent pathogen attack [36].This outcome is analogous to that resulting from immunization or pre exposure to a pathogen in animals, where the defense system is primed to improve resistance to subsequent challenge by the pathogen. The jasmonate (or lipoxygenase) pathway mentioned above involves oxygenation of fatty acids, and a similar pathway known as the eicosanoid (e.g., prostaglandins and leukotrienes) pathway is present in mammals. Oxylipins, end products of these pathways, are implicated in host defense and stress responses. These molecules are also present in fungi and involved in signaling and development [37].

3.3 Programmed Cell death and Oxidative Burst

Commonalities of the defense systems of different hosts against fungal pathogens include programmed cell death and oxidative burst response [38 and 39]. Animal and plant pathogenic microbes (fungal and bacterial) release molecules with pathogenicity – associated molecular patterns. Determinants on fungus – derived polysaccharides and proteins are recognized (usually indirectly) by conserved receptors in animals and plants and elicit a defense response. These receptors are often transmembrane proteins with leucine – rich repeat domains and are manifested as resistance gene products in plants and Toll – interleukin receptors in animal and insect cells (8). This appears to be either an ancient conserved eukaryotic pathway [40] or the result of convergent evolution whereby similar motifs have been recruited for defense in different systems [41].

The suicide of individual cells is an efficient and conserved mechanism to achieve and maintain homeostasis in multicellular organisms as a response to pathogen attack and abiotic stress, as well as in normal development [42]. The selective elimination of certain cells is carried out by a gene – directed process called programmed cell death that is mentioned above. This is an energy dependent asynchronic process that comprises the loss of cell – to – cell contacts, cytoplasmic shrinkage, membrane blebbing, DNA fragmentation, disassembly of the nuclei and formation of apoptotic bodies. The execution of programmed cell death requires the participation of complex cell suicide machinery that involves several molecules regulated by the expression of a certain set of genes. The self – contained nature of programmed cell death contrasts with necrosis, which is an unregulated process of traumatic destruction, followed by the release of intracellular components without the active participation of the cell [43]. In animals, the active study of programmed cell death began in 1972 when Kerr et al. introduced the term apoptosis as "a basic biological phenomenon with a wide range of implications in tissue kinetics" [44]. However, it took more than a decade to realize the biological importance of programmed cell death in plant pathogenesis and development [45]. As in animals, programmed cell death plays a key role in numerous vegetative and reproductive phases of plant development, including the senescence of leaves, xylogenesis, death of petals after fertilization, postembryonic decay of aleuronic layers, root cap development, somatic and zygotic embryogenesis and sex determination. Similarly, programmed cell death in plants occurs in response to biotic and abiotic stimuli. In plant pathogen interactions, programmed cell death serves not only as a defense mechanism of the plant in incompatible interactions, but also to promote the dissemination of the pathogen in compatible interactions [46]. Avirulent infections are usually characterized by a localized cell death known as hypersensitive response (HR) which results in the formation of necrotic lesions around the infection sites [47]. On the other hand, there is the abiotic stress response, and the best example is aerenchyma development under low oxygen conditions, in which root cortical cells are induced to die and form larger airspaces, enabling a greater diffusion of air from the upper parts of the plant [48]. Programmed cell death in plants has also been characterised in response to high temperature [49]. Finally, some of the morphological features of apoptosis as well as transduction pathways and signal molecules have been shown to be similar in both animals and plants. However, differences in the execution of Programmed cell death have also been observed.

Oxidative burst response is a phenomena that include the production at the cell surface of different molecules such as: hydrogen peroxide (H_2O_2), superoxide (O_2^-), singlet oxygen (O_2) and hydroxyl radical (OH^-). Specifically, against microorganisms a sophisticated sensory system enables them to perceive chemical signals from potential pathogens and to translate them into appropriate biochemical responses [50 and 51].In biological systems 'oxidative stress' results from the presence of elevated levels of oxidizing agents that are able to abstract electrons from essential organic molecules and disturb cellular functions. Under normal conditions reactive oxygen species (ROS) appear in cells as unwelcome harmful by – products formed as a result of successive one – electron reductions of molecular oxygen [52]. As a consequence of disturbances in the normal redox state of the cell ROS molecules are produced, which have a toxic effect on it and damage all components inside them including proteins, lipids, and DNA. The magnitude of this damage depends upon the size of these changes, with a cell being able to overcome small perturbations and regain its original state. Most plant cells possess facing an even greater burden of ROS has the ability to detoxify it and have also acquired the relevant protective mechanisms to maintain the lowest possible levels of ROS inside. To these protective mechanisms belong some antioxidant molecules (tocopherol, ascorbate (ASC), glutathione (GSH), proline, betaine and carotenoids) and antioxidant enzymes like superoxide dismutase (SOD), ascorbate peroxidase (APX) and catalase (CAT). However, more severe oxidative stress can cause cell death and even moderate oxidation can trigger apoptosis, while more intense stresses may cause necrosis [53 and 54]. It is known that one of the earliest of many diverse defense reactions activated in plant tissues in response to pathogen attack, is the rapid and transient accumulation of huge amounts of ROS and depending on the interaction, these ROS – generating mechanisms involve plasma membrane NADPH oxidases or cell – wall peroxidases [55].Studies related with the role of ROS during plant pathogen interaction have been carried out in all kind of interactions. In hemibiotrophic interaction by [56; 57 and 58], in necrotrophic interaction by [59; 60; 61 and 62] and in biotrophic interaction by [63 and 64]. Besides another ones regarding to this theme have been done by [65; 66; 67; 68 and 69]. In spite of this plethora of information about ROS role in different plant – pathogen interactions, knowledge is still scarcely and not enough for a complete understanding of the oxidative stress in plants although, it is believed that during an interaction a coordinated activation at the site of infection requires tight control of the production of ROS, such as $H_2O_2$and O_2^- . Besides, some research has indicated that the ROS produced in the oxidative burst could serve not only as protectant against invading pathogen, but could also be the signals activating further plant defense reactions [70].

Mammals in general, as well as most of their organs, are quite intolerant of anoxia and/or ischemia partly because their metabolism is ill – equipped to endure the energy shortfall that occurs when mitochondrial ATP production is blocked and

partly because of injuries that arise due to a burst of ROS formation when oxygen is reintroduced. Clearly, in mammalian systems, the antioxidant defenses of the organism can be over whelmed by rapid and large changes in tissue ROS levels. However, although unusual for most mammals, many organisms routinely experience wide variation in oxygen availability to their tissues due to factors such as environmental oxygen lack, breath hold diving, extracellular freezing, or apneic breathing patterns in arrested metabolic states. To cope with these situations, many lower vertebrates and invertebrates have well – developed tolerances for anoxia and ischemia that allow them to endure these stresses as part of their normal life [71]. For example, various gill breathing intertidal marine invertebrates routinely experience cyclic bouts of oxygen deprivation with the tides and have evolved excellent capacities for facultative anaerobiosis that, in fact, allow them to survive for days or weeks at a time without oxygen [72]. Among vertebrates, anoxia tolerance is highly developed in various species of freshwater turtles that dive routinely and also hibernate underwater; species of the *Chrysemys* and *Trachemys* genera, for example, can survive for 3 – 4 months submerged in deoxygenated water at 30º C [73 and 74]. Freeze – tolerant animals have to deal not only with anoxia but also with ischemia for when extracellular body fluids freeze, all circulation is cut off and individual cells must rely on internal fermentative fuel reserves to survive for perhaps days or weeks until they thaw again. Freeze tolerance is quite common among cold – hardy insects in northern latitudes and is also a strategy used by several species of woodland frogs and some hatching turtles for winter survival [75]. In addition, many other types of animals, while not facing such extremes of anoxia or ischemia, experience wide variation in oxygen availability in their normal life and endure wide cycles of normoxic and hypoxic conditions. For example, estivating animals (such as various land snails and burrowing toads) have this experience since they use apnoeic breathing patterns to minimize body water loss during longterm dormancy [76 – 78] and diving animals (such as seals and whales) experience profound hypoxia in many organs due to circulatory readjustments that preferentially direct oxygenated blood to the skeletal muscles and brain [79]. Hibernating mammals also experience hypoxia due to apnoeic breathing while dormant and experience a rapid 10 – 20 – fold increase in oxygen consumption during arousal when they rewarm their bodies from ambient back to 37ºC over just a few minutes [80].

IV. PARALLELS IN PATHOGENESIS ON PLANT AND ANIMAL HOST

4.1 Fungus

The best studied fungal isolate that can affect both animals and plants is *Fusarium oxysporum* f. sp. *lycopersici*, which can kill both immunodepressed mice and tomato plants [81]. Studies of this fungus highlight commonalities and differences in the mechanisms of pathogenicity on animal and plant hosts. For example, a mitogen – activated protein (MAP) kinase gene, Fmk1, of *F. oxysporum* is not required for virulence in mice but is essentialfor virulence in tomatoes. In contrast, the zinc finger transcription factor gene PacC is necessary for full virulence in mice but not in tomatoes [81]. PacC is important for virulence in a range of other plant – specific and animal – specific fungi, as it mediates the environmental pH signal, which in turn alters gene expression appropriately. Another soilborne fungus, *Aspergillus flavus*, can infect animals, insects, and plants, particularly seeds of corn, peanuts, cotton, and nut trees. This fungus, like several other *Aspergillus* species, produces highly toxic, carcinogenic aflatoxins. Several strains isolated from humans and insects can also cause disease in corn [82]. Different nutritional pathways may be important for the virulence of this fungus on different hosts, since a cysteine and methionine auxotroph of *A. flavus* has reduced conidiation in vitro and on plant hosts, but this auxotroph can still complete a disease cycle on insect hosts [83].

4.2 Bacteria

The genus *Salmonella* consists of only two species, *S. bongori* and *S. enterica*, and the latter is divided into six subspecies. *Enterica* includes more than 1,500 serotypes, which despite their high genetic similarity vary greatly in their host range and disease outcome ranging from enteritis to typhoid fever [84].*Salmonella enterica* subsp. *enterica*is an important economic and public health problem throughout the world. The degree of adaptation to hosts varies between *Salmonella* serotypes and determines the pathogenicity. Serotypes adapted to humans, such as *S. typhi* and *S. paratyphi* A, B, C, cause systemic typhoid fever. These serotypes are not pathogenic for animals. Similarly, *S. gallinarum* and *S. abortusov*is, which are specifically adapted to poultry and ovine, respectively, are responsible for severe systemic infections in these animals. However, *S. choleraesuis*, for which pigs are the primary hosts, also causes severe systemic illness in humans. Ubiquitous serotypes, such as S. *enteritidis* or *S. typhimurium*, generally cause gastrointestinal infections in humans but can induce other diseases in animals [85]. For example, they can produce typhoid – like infections in mice, systemic infection in humans or asymptomatic intestinal colonization in chickens and pigs [86]. Some of them are responsible for chlorosis on plant leaves sometimes causing death [87; 88, 89 and 90]. Disease in mammals occurs after ingestion of contaminated food or water. *Salmonella* infection of animals and humans depends on the ability of bacteria to survive the harsh conditions of the gastric

tract before entering the intestinal epithelium and subsequently colonizing the mesenteric lymph nodes and internal organs in the case of systemic infections. In order to enter non – phagocytic cells and survive within the host environment, *Salmonella* has evolved mechanisms to interact with host cells and to induce its own internalization [91 and 92] *Salmonella* usually enters agricultural environments via animal feces. Animals can directly contaminate plants or surface water used for irrigation and pesticide or fertilizer diluent through contaminated feces. Recently, there has been an increasing number of reports, linking *Salmonella* contaminated raw vegetables and fruits with food poisoning [93]. *Salmonella* is able to adapt to different external conditions including low pH or high temperature, allowing it to survive outside the host organism [94 and 95]. Indeed, *Salmonella* is able to attach and adhere to plant surfaces before actively infecting the interior of different plants, leading to colonization of plant organs [96 and 97], and suppression of the plant immune system [98]. In addition, *Salmonella* originating from plants retains virulence toward animals [89]. Thus, plants are an alternative host for *Salmonella* pathogens, and have a role in its transmission back to animals.

4.3 Viruses

Unlike animal viruses, plant viruses cannot replicate in humans or other animals, largely due to the lack of specific receptors for recognition and entry into host cells. However, it has been demonstrated that cowpea mosaic virus enters the bloodstream in mice from the intestine when administrated in cowpea leaves and induces the production of antibodies without replicating [99; 100; and 101]. More recently, a case – control study showed that pepper mild mottle virus may be found in human feces and is associated with clinical immune responses [102]. These studies suggest that plant viruses may play a role in human health and disease. Until now, the possible effects of consumption of TMV (tomato mosaic virus) in tobacco products have not been investigated. Tobacco smoking has been shown to cause cancers [103], heart disease [104], and chronic obstructive lung disease [105]. It also increases the risk for development of multiple autoimmune disorders such as rheumatoid arthritis [106] and multiple sclerosis [107; 108 and 109] Although the health risks of tobacco smoking are well documented, increasing evidence suggests that smokers have a lower incidence of some inflammatory and neurodegenerative diseases. For example, smoking is reported to reduce human autoimmune responses in systemic lupus erythematosus [119] and ulcerative colitis [111]. Of particular interest to neurodegenerative disorders, epidemiological studies consistently show smokers to have a lower risk of developing Parkinson's disease [112 and 113,] which is associated with a long duration of smoking rather than smoking intensity [114]. Such an inverse association is also observed in people who use chewing tobacco [115]. The protective effects of smoking have been suggested to result from the ability of nicotine (the main addictive ingredient of tobacco) to inducing immunosuppression [108] and neuroprotective action [116 and 117] but the biological mechanisms by which this occurs remain largely unclear. As a complex mixture of more than 4,700 chemical compounds, many constituents of cigarettes have been shown to modulate immune function including both the humoral and cell – mediated immune responses [108]. Tobacco mosaic virus can survive for years in cigars and cigarettes made from infected tobacco leaves, and TMV can be found on the surface of cigarettes. Therefore, we presume that smokers are more likely to be exposed to TMV than non – smokers. We tested whether exposure to tobacco products induces immune responses o TMV in humans and compared the differences among individuals who were smokers, smokeless tobacco users and nonsmokers. Identification of mechanisms for TMV – elicited specific immune responses may aid in defining the etiology and pathogenesis of smoking – related human diseases. It has also proven that the human protein TOMM40L (an outer mitochondrial membrane 40 homolog – like translocase) contains a strong homology of six contiguous amino acids to the TMV coat protein, and TOMM40L peptide exhibited cross – reactivity with anti – TMV antibodies. There is a mimicry between TMV and human TOMM40L that is caused to raising the question as to whether TMV has a potential role in smokers against Parkinson's disease development.

The potential mechanisms of molecular mimicry between plant viruses and human disease should be further explored [118].

V. CONCLUSION

Whereas living organisms are very different, on the other hand are very similar. These differences and similarities include relationship between them and the methods of their defense against their pathogens. The most important difference between plants and animals is absence of circulatory system and an adaptive immune system in plants. In both plants and animals the first step in the recognition of a pathogen is a general response, when non – specific receptors on the surface of plant or animal cells detect non – specific PAMPs (pathogen – associated molecular patterns). These molecules regularly occur in bacteria, fungi and in several other microbes. Plant do not have immune system that is the base of immunity in animals so how can plants recognize a high number of effectors of pathogenic races? The answer is "gene – for – gene concept". In each

incompatible (resistant) host/pathogen combination an avirulence gene encodes a specific effector and a plant r – gene encodes a specific receptor.

REFERENCES

[1] C.B. Tylor, ''Defense Responses in Plants and Animals – More of the Same,'' The Plant Cell, vol. 10, pp. 873 – 876, June 1998.

[2] R. Koch, ''Die Aetiologie der Milzbrandkrankheit, begrundet auf der Entwicklungsgeschichte des,'' Biol. Pflanzen, vol. 2, pp. 277 – 310, 1986.

[3] T.J. Burill, ''Remarks made in a discussion,'' Trans. III. State. Hortic. Soc. [N.S.] vol. 11, pp. 79 – 80, 1878.

[4] G. Felix, J. D. Duran, S.Volko, and T. Boller, ''Plants have a sensitive perception system for the most conserved domain of bacterial flagella,''. Plant. J, vol. 18, pp. 265 – 276, 1999.

[5] F. M. Ausubel, ''Are immune signaling pathways in plants and animals conserved?'' Nature, Immunol, vol. 6, pp. 973 – 979, 2005.

[6] J.P. Rast, L.c. Smith, M. Loza – coll, T. Hibino, and G. W. Litman, ''Genomic insights into the immune system of the sea urchin,'' Science, vol. 314, pp. 952 – 956. 2006.

[7] T. Boller, and G. A. Felix, ''A renaissance of elicitors: perception of microbe – associated molecular patterns and danger signals by pattern – recognition receptors,'' Annul. Rev. Plant Biol, vol. 60, pp. 379 – 406, 2009.

[8] P.C. Ronald, B. and Beutler, ''Plant and animal sensors of conserved microbial signatures,'' Science, vol. 330, pp. 1061 – 1064. 2010.

[9] A. M. Ones, and J. L. Dangl, ''The plant immune system. Nature, vol. 444, pp. 323 – 329, 2006.

[10] C. Zipfel, J. P. and rathjen, ''Plant immunity: AvrPto targets the frontline,'' Curr. Biol, vol. 18, pp. 218–220, 2008.

[11] S.D. Kale, B. Gu, D. G. Capelluto, D. Dou, ''External lipid PI3P mediates entry of eukaryotic pathogen effectors into plant and animal host cells,''Cell, vol. 142, pp. 284–295, 2010.

[12] A.f. Ross, ''Systemic acquired resistance induced by localized virus infections in plants,'' Virology, vol. 14, pp. 340–358, 1961.

[13] W.E. Durrant, and X. Dong, ''Systemic acquired resistance,'' Annul. Rev. Phytopathology, vol. 42, pp. 185 –209, 2004.

[14] S.H. Spoel, and X. Dong, ''How do plants achieve immunity defense without specialized immune cells,'' Nature. Rev. Immunol, vol. 12, pp. 89 – 100.

[15] H.H Flor, ''Current status of the gene for gene concept,'' Annul. Rev. Phytopatol, vol. 9, pp. 275 – 296, 1971.

[16] J. Liu, J. M. Elmore, Z.J.D. Lin, and G. Coaker, ''A receptor – like cytoplasmic kinase phosphorylates the host target rIn4, leading to the activation of a plant innate immune receptor,'' Cell. Host. Microbe, vol. 9, pp. 137–146. 2011.

[17] E.H. Chung, L. da Cunha, A. J. Wu, Z. Gao, K. Cherkis, A. J. Afzal, D. Mackey, and J.L. Dangl, ''Specific threonine phosphorylation of a host target by two unrelated type III effectors activates a host innate immune receptor in plants,''Cell. Host. Microbe,vol. 9, pp. 125–136, 2011.

[18] M.S. Mukhtar, A.R. Carvunis, M.N. Dreze, and P. Epple, ''Independently evolved virulence effectors converge onto hubs in a plant immune system network,''Science, vol. 333, pp. 596–601, 2011.

[19] Y. Tao, Z. Xie, W. Chen, J. Glazebrook, H.S. Chang, B. Han, T. zhu, G. Zou, and F. Katagiri, '' Quantitative nature of *Arabidopsis* responses during compatible and incompatible interactions with the bacterial pathogen *Pseudomonas syringae*,''. Plant cell, vol. 15, pp. 317 – 330, 2003.

[20] L. Navarro, C. Zipfel, O. Rowland, I. Keller, S. Robatzek, T. Boller, and J.D.G. Jones, ''The transcriptionalinnate immune response to flg22. Interplay and overlap with Avr gene – dependent defense responses and bacterial pathogenesis, Plant Physiol, vol. 135, pp. 1113 – 1128, 2004.

[21] C. Zipfel, S. Robatzek, L. Navarro, E.J. Oakeley, J.D.G. Jones, G. felix, and T. Boller, ''Bacterial disease resistance in *Arabidopsis* through flagella perception,''Nature, vol. 428, pp. 764–767. 2004.

[22] A.M. Jones, and J.L. Dangl, ''The plant immune system, Nature, vol. 444, pp. 323 – 329, 2006.

[23] J.R. Alfano, and A. Collmer, A. ''Type III secretion system effector proteins: double agents in bacterial disease and plant defense,'' Annul. Rev. Phytopathol, vol. 42, pp. 385 – 414, 2004.

[24] P. Matzinger, ''The danger model: A renewed sense of self, '' Science, vol. 296, pp. 301–305, 2002.

[25] M.G. Netea, J. Quintin, and J.W. van der Meer, ''Trained immunity: A memory for innate host defense,''Cell Host Microbe, vol. 9, pp. 355–361, 2011.

[26] C. Darwin, ''On the Origin of Species by Means of Natural Selection, or the Preservation of Favored Races in the Struggle for Life,'' John Murray, London, 1859.

[27] R.H. Whittaker, ''On the broad classification of organisms,'' Quart Rev Biol, vol. 34, pp. 210 – 226, 1959.

[28] C.R. Woese, and G.E. Fox, ''Phylogenetic structure of the prokaryotic domain: the primary kingdoms,'' Proc Natl Acad Sci, USA, vol. 74, pp. 5088 – 5090, 1977.

[29] C.R. Woese, O. Kandler and M.L. Wheelis,''Towards a natural system of organisms: proposal for the domains Archaea, Bacteria, and Eucarya,''. Proc Natl Acad Sci, USA,vol. 87, pp. 4576–4579, 1990,

[30] T. Cavalier – Smith, ''Eukaryote kingdoms: seven or nine,'' Bio systems, vol. 14, pp. 461 – 481, 1981.

[31] T. Cavalier – Smith, ''Only six kingdoms of life,'' Proc R Lond, B, vol. 271, pp. 1251 – 1262, 2004.

[32] M.E. Vianna, G. Conrads, B.P. Gomes, and H.P. Horz, ''Identification and quantification of archaea in primary endodontic infections,'' J Clin Microbiol, vol. 44, pp. 1274 – 1282, 2006.

[33] R. Roozendaal, and M. Carroll, ‘‘Emerging patterns in complement mediated pathogen recognition,’’ Cell, vol. 125:pp. 29 – 32, 2006.

[34] C. Speth, G. Rambach, C. Lass – Florl, M. P. Dierich, and R. Wurzner., ‘‘The role of complement in invasive fungal infections,’’ Mycoses, vol. 47, pp. 93–103, 2004.

[35] J. H. Chu, C. Feudtner, K. Heydon, T. J. Walsh, and T. E. Zaoutis, ‘‘Hospitalizations for endemic mycoses: a population-based national study,’’ Clin. Infect. Dis, vol. 42, pp. 822 – 825, 2006.

[36] C.M. Pieterse, and L. Van Loon, ‘‘NPR1: the spider in the web of induced resistance signaling pathways. Curr. Opin. Plant Biol, vol. 7, pp. 456–464, 2004.

[37] J.M. Shea, and M. Del Poeta, ‘‘Lipid signaling in pathogenic fungi,’’ Curr. Opin. Microbiol, vol. 9, pp. 352–358, 2006.

[38] L.A. Mur, T. Carver, and E. Prats, ‘‘NO way to live; the various roles of nitric oxide in plant – pathogen interactions,’’ J. Exp. Bot, vol. 57, pp. 489–505, 2006.

[39] F.R. Nascimento, V. Calich, D. Rodriguez, and M. Russo, ‘‘Dual role for nitric oxide in paracoccidioidomycosis: essential for resistance, but over production associated with susceptibility, J. Immunol, vol. 168, pp. 4593 – 4600, 2002.

[40] T. Nrnberger, F. Brunner, B. Kemmerling, and L. Piater, ‘‘Innate immunity in plants and animals: striking similarities and obvious differences,’’ Immunol. Rev, vol. 198 pp. 249 – 266, 2004.

[41] F. Ausubel, ‘‘Are innate immune signaling pathways in plants and animals conserved?’’ Nat. Immunol, vol. 6, pp. 973 – 979, 2005.

[42] D.G. Gilchrist, ‘‘Programmed cell death in plant disease: the purpose and promise of cellular suicide,’’Annul Rev Phytopathol, vol. 36, pp. 393 – 414,1998.

[43] H Okada, T.W. Mak, ‘‘Pathways of apoptotic and non-apoptotic death in tumours cells,’’ Nature Reviews, vol. 4, pp. 592 – 603, 2004.

[44] J.F.R. Kerr, A.H. Willie, A.R. Currie, ‘‘Apoptosis: a basical phenomenon with wide ranging implications in tissue kinetics,’’ Br J Cancer, vol. pp. 26, 239 – 257, 1972.

[45] R.I. Pennel, C. Lamb, ‘‘Programmed cell death in plants,’’ Plant Cell, vol. 9, 1157 – 1168, 1997.

[46] S.M.P. Urana, S.K. Pandey,D. Sarkas, A. Chanemougasoundharam, ‘‘Apoptosis in plant disease response:a close encounter of the pathogen kind,’’ Curr Sci, vol. 88, pp. 740 – 752, 2005.

[47] R.N. Goodman, A.J. Novacky, ‘‘The hyper sensitive reaction in plants to pathogens: a resistance phenomenon,’’ Amer Phyto pathol Soc, Press, St. Paul, 1996.

[48] M.C. Drew, C.J. He, P.W. Morgan, ‘‘Programmed cell death and aerenchyma formation in roots. Trends in Plant Science, vol. 5, pp. 123 – 127, 2000.

[49] P.F. McCabe, C.L. Leaver, ‘‘Programmed cell death in cell cultures. Plant Molecular Biology vol. 44, 359 – 368, 2000.

[50] P. Wojtaszek, ‘‘Oxidative burst: an early plant response to pathogen infection,’’ Biochem. J, vol. 322, pp. 681 – 692, 1997.

[51] J.T. Hancock,R. Desikan, and S.J. Neill, ‘‘Role of reactive oxygen species in cell signalling and development,’’ Nature Reviews Molecular Cell Biology, vol. 5, pp. 305 – 315, 2001.

[52] S.W. Ryter, H.P. Kim, A. Hoetzel, J.W. Park, K. Nakahira, X. Wang,A.M.K. Choi, ‘‘Mechanisms of cell death in oxidative stress,’’ Antioxidants & Redox Signalling, vol. 9(1), pp. 49 – 89, 2007.

[53] M.A. Torres, J.D.G. Jones, J. L. Dangl, ‘‘Reactive oxygen species signaling in response to pathogens. Plant Physiology, vol. 141, pp. 373 – 378, 2006.

[54] N.P. Shetty, H.J. Lyngs Jǿrgensen J. Due Jensen, D.B. Collinge, H. Shekar Shetty, ‘‘Roles of reactive oxygen species in interactions between plants and pathogens,’’ European Journal of Plant Pathology, vol. 121, pp. 267 – 280, 2008.

[55] M.A. Torres, ‘‘ROS in biotic interactions,’’ Physiologia Plantarum, vol.138, pp. 414 – 429, 2010.

[56] A.J. Able, D.I. Guest, M.W. Sutherland, ‘‘Hydrogen peroxide yields during the incompatible interaction of tobacco suspension cells inoculated with Phytophthora nicotianae,’’ Plant Physiology, vol. 124, pp. 899 – 910, 2000.

[57] C. Pignocchi, G. Kiddle, I. Hernande, S.J. Foster, A. Asensi, T. Taybi, J. Barnes, C.H. Foyer, ‘‘Ascorbate oxidase – dependent changes in the redox state of the apoplast modulate gene transcript accumulation leading to modified hormone signaling and orchestration of defense processes in tobacco,’’ Plant Physiology, vol. 141, pp. 423 – 435, 2006.

[58] N.P. Shetty, R. Mehrabi, H. Lutken,A. Haldrup, G.H.J. Kema,D.B. Collinge, H.J.L. Jorgensen, ‘‘Role of hydrogen peroxide during the interaction between the hemibiotrophic fungal pathogen *Septoria tritici* and wheat,’’ New Phytologist,vol. 174, pp. 637 – 647, 2007.

[59] C. Garca – Limones, A. Hervas, J.A. Navas – Cortes, R.M. Jimenez – Daaz and M. Tena, ‘‘Induction of an antioxidant enzyme system and other oxidative stress markers associated with compatible and incompatible interactions between chickpea,’’ Physiological and Molecular Plant Pathology, vol. 61, pp. 325 – 337, 2002.

[60] D.R. Davies, L.V. Bindschedler, T.S. Strickland, G.P. Bolwell, ‘‘Production of reactive oxygen species in *Arabidopsis thaliana* cell suspension cultures in response to an elicitor from *Fusarium oxysporum*: implications for basal resistance,’’ Journal of Experimental Botany, vol. 57(8), pp. 1817 – 1827, 2006.

[61] B. Asselbergh,K. Curvers, S.C. Frana, K. Audenaert, M. Vuylsteke, F. Van Breusegem,M.M. Hofte, ‘‘Resistance to *Botrytis cinerea* in sitiens, an abscisic acid – deficient tomato mutant, involves timely production of hydrogen peroxide and cell wall modifications in the epidermis,’’ Plant Physiology, vol. 144, pp. 1863 – 1877, 2007.

[62] C. Garcia – Limones G. Dorado, J.A. Navas – Cortes, R.M. Jimenez –Diaz, and M. Tena, ‘‘Changes in the redox status of chickpea roots in response to infection by *Fusarium oxysporum* f. sp. *ciceris*: apoplastic antioxidant enzyme activities and expression of oxidative stress – related genes, ’’ Plant Biology, vol. 11, pp. 194 – 203, 2009.

[63] U. Bechtold, S. Karpinski, P.M. Mullineaux, 'The inuence of the light environment and photosynthesis on oxidative signalling responses in plant–biotrophic pathogen interactions,'' Plant, Cell and Environment, vol. 28, pp. 1046 – 1055, 2005.

[64] D. Romero, M.E. Rivera, F.M. Cazorla, J.C. Codina, D. Fernandez – Ortuno, J.A. Tores, Perez – Garcia, A. de Vicente,''Comparative histochemical analyses of oxidative burst and cell wall reinforcement in compatible and incompatible melon–powdery mildew *Podosphaera fuscainteraction,*'' Journal of Plant Physiology, pp. 1 – 11, 2008.

[65] L.V. Bindschedler, J. Dewdney, K.A. Blee, J.M. Stone, T. Asai, J. Plotnikov, C. Denoux, T. Hayes, C. Gerrish, D.R. Davies, F.M. Ausubel, G.P. Bolwell,''Peroxidase-dependent apoplastic oxidative burst in *Arabidopsis* required for pathogen resistance,'' The Plant Journal, pp. 1 – 13, 2006.

[66] M.A. Torres, J.D.G. Jones, J.L. Dangl, ''Reactive oxygen species signaling in response to pathogens. Plant Physiology''vol. 141, pp. 373 – 378, 2006.

[67] E. D, Zago, S. Morsa, J.F. Dat, P. Alard, A. Ferrarini, D. Inze, M. Delledonne, F. Van Breusegem, ''Nitric oxide – and hydrogen peroxide responsive gene regulation during cell death induction in tobacco,'' Plant Physiology, vol. 141(2), pp. 404 – 411

[68] H.W. Choi, Y. J. Kim, S.C. Lee, J.K. Hong, B.K. Hwang, ''Hydrogen peroxide generation by the pepper extracellular peroxidase CaPO2 activates local and systemic cell death and defense response to bacterial pathogens,'' Plant Physiology, vol. 145, pp. 890 – 904, 2007.

[69] N.P. Shetty, H.J. Lyngs Jǿrgensen, J. Due Jensen, D.B. Collinge, H. Shekar Shetty, ''Roles of reactive oxygen species in interactions between plants and pathogens, '' European Journal of Plant Pathology, vol. 121, pp. 267 – 280, 2008.

[70] F. Van Breusegem, J. Bailey – S Serres, R. Mittler, ''Unraveling the tapestry of networks involving reactive oxygen species in plants,'' Plant Physiology, vol. 147, pp. 978 – 984, 2008.

[71] P.L. Lutz, and K.B. Store ''Adaptations to variations in oxygen tension by vertebrates and invertebrates,'' In: Lutz PL & Storey KB (Editors), Handbook of Comparative Physiology, CRC Press, Boca Raton, 1996.

[72] K.B. Storey ''Molecular mechanisms of metabolic arrest in mollusks,'' In: Hochachka PW, Lutz PL, Sick TJ, Rosenthal M & van den Thillart G (Editors), Surviving Hypoxia: Mechanisms of Control and Adaptation. CRC Press, Boca Raton, 1993.

[73] G.R. Ultsch, GR''Ecology and physiologyof hibernation and overwintering amongfreshwater fishes, turtles and snakes, '' BiologicalReviews, vol. 64, pp. 435 – 516. 1989.

[74] K.B. Storey, ''Metabolic adaptationssupporting anoxia tolerance in reptiles: recent advances,'' Comparative Biochemistryand Physiology B, vol. 113, pp. 23 – 35. 1996.

[75] K.B. Storey, D.D. Mosser, D.N. Douglas,J.E. Grundy, and J.M. Storey, ''Biochemistrybelow OC: nature's frozen vertebrates,'' Brazilian Journal of Medical andBiological Research, vol. 29, pp. 293 – 307. 1996.

[76] J.P Loveridge, and P.C. Withers,''Metabolismand water balance of active andcocooned African bullfrogs *Pyxicephalusadspersus*,'' Physiological Zoology, vol. 54, pp. 203 – 214. 1981.

[77] M.C. Barnhart, ''Discontinuous carbondioxide release and metabolic depression in dormant land snails. JournalofExperimentalBiology, vol. 128, pp. 123 – 138, 1987.

[78] A.W. Pinder, K.B. Storey, and G.R. Ultsch, ''Estivation and hibernation, ''. In: Feder MEand Burggren WW (Editors), EnvironmentalBiology of the Amphibia. University ofChicago Press, Chicago, 1992.

[79] P.W. Hochachka,and G.N. Somero, ''Biochemical Adaptation,'' Princeton UniversityPress,Princeton, 1984.

[80] L.C.H. Wang, ''Ecological, physiological,and biochemical aspects of torpor inmammalsand birds,'' In: Wang LCH (Editor),Advances in Comparative and EnvironmentalPhysiology, Vol. 4, SpringerVerlag,Heidelberg, 1989

[81] M.J. Ortoneda, M.P. Guarro, Z. Madrid, M.I.G. Caracuel, E. Roncero Mayayo, and A. Di Pietro, ''*Fusarium oxysporum* as a multihost model for the genetic dissection of fungal virulence in plants and mammals,'' Infect. Immun, vol. 72, pp. 1760 – 1766, 2004.

[82] R.J. St. Leger, S. E. Screen, and B. Shams – Pirzadeh, ''Lack of host specialization in Aspergillus flavus. Appl. Environ. Microbiol, vol. 66, pp. 320 – 324. 2000.

[83] L. Scully, and M. Bidochka, ''A cysteine/methionine auxotroph of the opportunistic fungus Aspergillus flavus is associated with host-range restriction: a model for emerging diseases,'' Microbiology, vol. 152, pp. 223 – 232, 2006.

[84] M.E. Ohl, and S.I. Mille, ''Salmonella: a model for bacterial pathogenesis,'' Annul. Rev. Med, vol. 52, pp. 259 – 274. 2001.

[85] K. Hoelzer, A.I. Moreno Switt, and M. Wiedmann, ''Animal contact as a source of human non – typhoidal salmonellosis. Vet. Res, vol. 42, 34, 201.

[86] P. Velge, A. Wiedemann, M. Rosselin, N. Abed, Z. Boumart, A. M. Chausse, ''Multiplicity of Salmonella entry mechanisms, a new paradigm for Salmonella pathogenesis, '' Microbiologyopen, vol. 1, pp. 243 – 258.

[87] M.M. Klerks, M. Van Gent – Pelzer, M., E. Franz, C. Zijlstra, andA.H.C. van Bruggen, ''Physiological and molecular response of *Lactuca sativa* to colonization by *Salmonella enterica* serovar Dublin, Appl. Environ. Microbiol, vol. 73, pp. 4905–4914,2007b.

[88] A. Schikora, A. Carreri, E. Charpentier, and H. Hirt, H. ''The dark side ofthe salad: *Salmonella Typhimurium* overcomes the innate immune response of*Arabidopsis thaliana* and shows an endopathogenic lifestyle,''. PLoS ONE vol. 28, 2008

[89] A. Schikora, I. Virlogeux – Payant, E. Bueso, A.V. Garcia, T. Nilau, A. Charrier, A., ''Conservation of *Salmonella* infection mechanisms in plants and animals,'' PLoS ONE, vol. 6, 2011

[90] G. Gu, J.M. Cevallos – Cevallos, and A.H. C. van Bruggen, ''Ingress of *Salmonella enterica* Typhimurium into tomato leaves through hydathodes. PLoS, 2013b.

[91] A. Vazquez – Torres, J. Jones – Carson, A.J. Baumler, S. Falkow, R. Valdivia, W. Brown, ''Extraintestinal dissemination of Salmonella by CD18 – expressing phagocytes,'' Nature, vol. 401, pp. 804–808, 1999.

[92] M. Rosselin, N. Abed, F. Namdari, I. Virlogeux – Payant, P. Velge, and A. Wiedemann, "The different strategies used by *Salmonella*to invade host cells in *Salmonella* – Distribution, Adaptation,'' Control Measures and Molecular Technologies, Chap. 17, eds B. A. Annous and J. B. Gurtler (Rijeka: InTech), pp. 339–364, 2012.

[93] J.C. Heaton, and K. Jones,''Microbial contamination of fruit and vegetables and the behavior of enteropathogens in the phyllosphere,'': a review,J. Appl. Microbiol, vol. 104, pp. 613–626, 2008.

[94] J. Samelis, J.S. Ikeda, and J.N. Sofos, ''Evaluation of the pHdependent, stationary – phase acid tolerance in *Listeria monocytogenes* and *Salmonella* Typhimurium DT104 induced by culturing in media with 1% glucose: a comparative study with *Escherichia coli* O157:H7,'' J. Appl. Microbiol, vol. 95, pp. 563–575, 2003.

[95] A.V Semenov,A.H. van Bruggen, L. van Overbeek, A.J. Termorshuizen, and A.M. Semenov, ''Influence of temperature fluctuations on *Escherichia coli* O157:H7 and *Salmonella enterica* serovar Typhimurium in cow manure. FEMS Microbiol. Ecol, vol. 60, pp. 419–428, 2007.

[96] M.M. Klerks, E. Franz, M. van Gent – Pelzer, M., C. Zijlstra, and A.H.C. van Bruggen, ''Differential interaction of *Salmonella enterica*serovars with *lettuce* cultivars and plant – microbe factors influencing the colonization efficiency,''ISME J, vol. 1, pp. 620–-631. 2007a

[97] G. Gu, J. Hu, J.M. Cevallos – Cevallos, S.M Richardson, J.A. Bartz, A.H. and van Bruggen, '' Internal colonization of *Salmonella enterica*serovar Typhimurium in tomato plants, '' PLoS ONE, vol. 6, 2011.

[98] A. Schikora, A.V. Garcia, and H. Hirt, ''Plants as alternative hosts for Salmonella,'' Trends Plant Sci, vol. 17, pp. 245–249, 2012.

[99] Q. Hu, Y. Niu, K. Zhang, Y. Liu, X. Zhou,''Virus – derived transgenes expressing hairpin RNA give immunity to Tobacco mosaic virus and Cucumber mosaic virus,''. Virol J, vol. 8, 41, 2011.

[100] L.P. Shriver, K.J Koudelka, M. Manchester, ''Viral nanoparticles associate with regions of inflammation and blood brain barrier disruption during CNS infection,''. J Neuroimmunol, vol. 211, pp. 66 – 72, 2009.

[101] W. Olszewska, M.W. Steward,''The molecular basis of the antigenic crossreactivity between measles and cowpea mosaic viruses, '' Virology,vol. 310, pp. 183 – 189, 2003.

[102] C.S. Rae, I.W. Khor, Q. Wang, G. Destito, M.J. Gonzalez, ''Systemic trafficking of plant virus nanoparticles in mice via the oral route,''. Virology, vol. 343,pp. 224 – 235, 2005.

[103] P. Colson, H. Richet,C. Desnues, F. Balique, V. Moal V, ''Pepper mild mottle virus, a plant virus associated with specific immune responses, Fever, abdominal pains, and pruritus in humans,'' PLoS One 5, e10041, 2010.

[104] N. Hymowitz,''Smoking and cancer: a review of public health and clinical implications,'' J Natl Med Assoc,vol. 103, pp. 695 – 700, 2011.

[105] J.J. Prochaska,J.F. Hilton ''Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta – analysis, BMJ, 344: e2856, 2012.

[106] N.R. Anthonisen,J.E. Connett, J.P. Kiley,M.D. Altose, W.C. Bailey,''Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1,'' The Lung Health Study, JAMA, 272: 1497 – 1505, 1994.

[107] F.W. Miller, L. Alfredsson K.H. Costenbader,D.L. Kamen, L.M. Nelson, LM, ''Epidemiology of environmental exposures and human autoimmune diseases,'' Findings from a National Institute of Environmental Health Sciences, Expert Panel Workshop. J Autoimmun, 2012

[108] M. Emre, C. de Decker,''Effects of cigarette smoking on motor functions in patients with multiple sclerosis,'' Arch Neurol,vol. 49,pp. 1243 – 1247, 1992.

[109] M. Sopori,''Effects of cigarette smoke on the immune system,'' Nat Rev Immunol, vol. 2, pp. 372 – 377, 2002.

[110] Y. Arnson,Y. Shoenfeld H. Amital ''Effects of tobacco smoke on immunity, inflammation and autoimmunity,'' J Autoimmun, vol. 34, pp. J258 – 265, 2010.

[111] R.L. Rubin, T.M. Hermanson, E.J. Bedrick, J.D. McDonald, S.W. Burchiel, ''Effect of cigarette smoke on autoimmunity in murine and human systemic lupus erythematosus,'' Toxicol Sci, vol. 87, pp. 86 – 96, 2005.

[112] S.S. Mahid, K.S. Minor, R.E. Soto, C.A. Hornung, S. Galandiuk,''Smoking and inflammatory bowel disease: a meta – analysis,''. Mayo Clin Proc, vol. 81, pp. 1462 – 1471, 2006.

[113] K.M. Powers,D.M. Kay,S.A. Factor, C.P. Zabetian, D.S. Higgins, ''Combined effects of smoking, coffee, and NSAIDs on Parkinson's disease risk,'' Mov Disord, vol. 23, pp. 88 – 95, 2008.

[114] H. Checkoway, K. Powers, T. Smith – Weller, G.M. Franklin,W.T. Longstreth,'' Parkinson's disease risks associated with cigarette smoking, alcohol consumption, and caffeine intake. Am J Epidemiol, vol. 155, pp. 732 – 7 38, 2002.

[115] H. Chen, X. Huang, X. Guo, R.B. Mailman, Y. Park,''Smoking duration, intensity, and risk of Parkinson disease,'' Neurology, vol. 74, pp. 878 – 884, 2010.

[116] B. Ritz, A. Ascherio, H. Checkoway, K.S. Marder, L.M. Nelson, ''Pooled analysis of tobacco use and risk of Parkinson disease,'. Arch Neurol, vol. 64, pp. 990 – 997, 2007.

[117] M. Quik, ''Smoking, nicotine and Parkinson's disease, '' Trends Neurosci, vol. 27, pp. 561 – 568, 2004.

[118] M. Quik, X.A. Perez, T. Bordia, ''Nicotine as a potential neuroprotective agent for Parkinson's disease. Mov Disord, vol. 27, pp. 947 – 957, 2010.

[119] R. Liu, R.A Vaishnav, A.M. Roberts, R.P. Friedland,''Humanshave Antibodies against a Plant Virus: Evidence from Tobacco Mosaic Virus,'' PLoS ONE vol. 8(4), 2013.