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Proteus mirabilis as a pathogenic organism

Umbreen Zafar[1], Muhammad Kamran Taj[2*], Imran Nawaz[1], Ashiq Hussain[3], Imran Taj[2], Zain-ul-Abideen[4], Sidra Mengal[1], Malala Panezai[1] , Nasir Ahmed Rind[2], Syeda Ayesha Ali[2], Ghulam Mohammad[2], Saima Azam[2], Zohra Samreen[3]

[1]*Department of Microbiology, University of Balochistan, Quetta, Pakistan*

[2]*Center for Advanced Studies in Vaccinology and Biotechnology, University of Balochistan, Quetta, Pakistan*

[3]*Bolon University of Medical and Health Sciences, Quetta, Balochistan*

[4]*Livestock and Dairy Development Department, Balochistan,Quetta, Pakistan*

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Abstract

Proteus is the member of family *Enterobacteriaceae*. They are gram negative, facultative anaerobic and rod shaped bacteria. *Proteus mirabilis* caused wounds infection, urinary tract infection, rheumatoid arthritis and meningitis in infants. Pathogenicity of *Proteus mirabilis* is facilitated by their unique virulence factors like adhesins, flagella, toxins, quorum-sensing, enzymes and immune invasion. The ability of urease gene of *Proteus mirabilis* that breakdown the urea into ammonia and carbon dioxide that increase the pH of urine resulting adherence, colonization, and biofilm formation. *Proteus mirabilis* are sensitive to most of β-lactams contaning antibiotics but also show resistance against broad spectrum β-lactamases, and AmpC enzymes when they acquired β-lactamases genes. *Proteus mirabilis* has been increased extended-spectrum β-lactamase (ESBL) production. The most predominant enzymes of *Proteus mirabilis* such as TEM, CTX-M ,VEB- and PER are less common. *Proteus mirabilis* express number of virulence factors that promote pathogenicity. This information about *Proteus* virulence will help to a better understanding of infectious processes and will allow to develop new effective procedure for prevention and clinical treatment.

* **Corresponding Author:** Muhammad Kamran Taj ✉ kamrancasvab@yahoo.com

Introduction

Proteus mirabilis was first discovered by Gustav Hauser in 1885. The name of *Proteus* comes from poem Homer's *Odyssey* by their shape-shifting character because the *Proteus* has ability to change their rod-shaped vegetative cell in to elongated and highly flagellated cell that has swarming motility (Mobley and Belas, 1995). *Proteus* is the member of family *Enterobacteriaceae*. The tribe *Proteeae is grouped* along with *Morganella, Providencia* genera (Antoni *et al*., 2012). This study is conducted to identify the virulance factors involve in pathogenesis of *Proteus mirabilis*.

Pathogenesis of Proteus mirabilis

Proteus mirabilis under suitable conditions has opportunity to cause wound infections, urinary tract infections, rheumatoid arthritis and meningitis in infants (Janda and Abbot, 2006). Pathogenicity of *Proteus mirabilis* is facilitated by their unique virulence factors and increase stay in human host (Christopher *et al*., 2000).

Virulence factor of Proteus mirabilis

Proteus mirabilis expresses several virulence factor involved in infection like adhesins, flagella, toxins, quorum-sensing, enzymes and immune invasion (Baldo and Rocha, 2014).

Fimbriae and adherence ability

Bacterial attachment to the epithelial surfaces play important role in virulence of urinary tract infections. Genomic analysis revealed that total of 17 potential fimbrial adhesins of *Proteus mirabilis* but, only 5 fimbriae have been studied (Pearson *et al*., 2008). Mannose-resistant/Proteus-like (MR/P), *Proteus mirabilis* fimbriae (PMF), uroepithelial cell adhesion (UCA), ambient-temperature fimbriae (ATF) and P. mirabilis P-like pili (PMP) (Rocha *et al*., 2007).

The important fimbriae of *P. mirabilis* is MR/P fimbriae. The MR/P gene is a group of two transcriptional genes *mrpI* and *mrpABCDEFGHJ* (mrp operon). The main structural subunit protein of *Proteus mirabilis* is MrpA protein.

PMF fimbriae having five functional genes *pmfACDEF*. The occurrence of mutantion is less important than its parent strain in uroepithelial cells, although colonization in kidney was not affected by *pmfA* mutation (Nielubowicz, 2010). The UCA/NAF fimbria has highly flexible rods that play an significant role in colonization of the urinary tract. The UCA operon has five genes PMI0532-PMI0536 of the genome sequence of HI4320 (Pelegrino *et al*., 2013). The ATF are important fimbriae in *Proteus mirabilis*. ATF fimbria show expression in 23°C and there is no difference between mutant and wild-type strain in urinary tract infection. Both of these fimbriae are not important in *P. mirabilis* host colonization (Zunino *et al*., 2000).

Enzymes

Urease is important enzyme in pathogenesis of *Proteus mirabilis*. Urease enzyme has ability of the formation of kidney and bladder stones and also block urinary tract. (Coker *et al*., 2000). The cluster of urease gene (ureRDABCEFG) that breakdown the urea into ammonia and carbon dioxide and increase the pH of urine. The change in pH can facilitate *P. mirabilis* adherence, colonization, and biofilm formation (Nicholson *et al*., 1991).

Toxins

Hemolysin

Hemolysin is a toxin that enter into host cell membranes and create pore in the membrane, resulting host cell damage (Braun and Focareta, 1991). This toxin facilitate Proteus in the kidney and also cause pyelonephritis in urinary tract. *P. mirabilis* has two hemolysin genes hpmA and hpmB. HpmA is present in the periplasm spaces, whereas HpmB is most likely present in outer membrane of host cell where it is involve in HpmA secretion process (Lukomski *et al*., 1991). However, the virulence of hemolysin is not completely understood (Mobley *et al*., 1991).

Proteus toxic agglutinin

This toxic protein is present in outer-membrane that facilitates cell to cell aggregation and the α-domain of

Proteus toxic agglutinin also has ability to lyse kidney and bladder cells. PTA gene of *P. mirabilis* had decrease pathology as well as, important colonization in the bladder, kidneys and spleen (Alamuri and Mobley, 2008).

Immune evasion

The presence of bacteria within host cell must evasion of primary and secondry immune responses. *Proteus mirabilis* encodes ZapA, that breaks the chain of immunoglobulins A1 (IgA1), IgA2 and IgG (Walker *et al*., 1999)

Mutation in zapA genes can decrease the immune system to find *Proteus mirabilis* in a host cell. Thus bacteria has ability to express different kind of fimbriae like MR/P and flagellin that increase adherence of bacteria to epithelial cell (Bahrani and Mobley,1994).

Swarming ability

Swarming behavior of proteus mirabilis is mediated by *rsbA* gene which RsbA may function as a protein sensor of environmental conditions (Manos and Belas, 2006). RsbA gene is also responsible in biofilm formation and extracellular polysaccharide formation (Liaw *et al*., 2004).

Biofilm formation

Biofilm formation due to *Proteus mirabilis* in urinary tract can increase the length of infection, and slow down activity of antibiotics and immune response. Thereby the bacteria is able to adhere uro-epithelial surfaces of host cell resulting accumulation of ammonia in uro-epithelial cells that becomes toxic and caused direct tissue damage (Sara, 2014). Stone formation by *P. mirabilis* in urinary tract can block the flow of urine through the catheter, bladder or kidneys that caused serious problems and also formation of pyelonephritis, septicemia, and shock. Diseases related to biofilm formation are chronic wounds infection, endocarditis, urinary tract infection, cystic fibrosis and periodontitis. biofilm formation can also weaken the immune system, thus bacteria can easily evade within the host. The PM1 strain has been shown to be able to form biofilm faster than PM2, and also is able to stimulate a lower inflammatory response (Parsek and Singh ., 2003).

Serotyping

The important virulence factor of *Proteus mirabilis* is lipopolysaccharide. The lipopolysaccharides some time explain the serology of bacteria. *Proteus mirabilis* are grouped into 80 O-serogroups. The OPS is acidic in all O-serogroups, by the presence of amino acids, uronic acids, phosphate, altruronic acid and other acidic nonsugar components (Knirel, 1999). *Proteus mirabilis* have branched or linear polysaccharides that madeup of repeating units oligosaccharide. However, *P. mirabilis* strains is belong to different serogroups such as, O3, O10, O11, O13, O23, O27, and O30 (Kaca *et al*., 2011).

Proteus mirabilis in urinary tract infection

Proteus mirabilis is capable to cause urinary tract infection such as cystitis, pyelonephritis and asymptomatic bacteriuria, mostly in type 2 diabetes patients. The infections of *Proteus mirabilis* also responsible for bacteremia and development of life-threatening urosepsis. Furthermore, *Proteus. mirabilis* can cause the formation of urinary stones (Matthews *et al*.,2011).

Proteus mirabilis in wound infection

Proteus mirabilis can cause wounds infection, specially in diabetic wounds along with *Klebsiella* species ,*E. coli*, *Enterobacter* species and *Serretia marscens* (Mutta *et al*., 2003). *Proteus mirabilis* are found in nosocomial infection. *Proteus mirabilis* cause clinical infections, so there is difficulty to elimate bacteria from host cell with complicated wounds infection, underlying diseases and the immuno-compromised patients (Auwaerter, 2008).

Proteus mirabilis in meningitis

Proteus mirabilis also involved in formation of neonatal sepsis and infections of the central nervous system. It is reported that only 4% cases of neonatal meningitis due to *Proteus mirabilis* (Unhanand *et al*., 1993). Cerebral abscess formation and

pneumocephalus has been described as also being associated with Proteus infections (Phan *et al*., 2012).

Antimicrobial susceptibility

Proteus mirabilis are sensitive to majority of antibiotics such as penicillin, cephalosporins, aminoglycosides, rifamycin and fluoroquinolones whereas resistant to amoxicillin, cefotaxime and carbenicillin (Saurina *et al*., 2000). *Proteus mirabilis* are sensitive to most of β-lactams contaning antibiotics because they do not show a chromosomally encoded AmpC cephalosporinase (Park *et al*., 2006). However, *Proteus mirabilis* show resistance against broad spectrum β-lactamases, and AmpC enzymes when they acquired β-lactamases genes (Andrea *et al*., 2006). Resistance of amoxicillin in *Proteus mirabilis* is mostly due to the TEM-1 and TEM-2 penicillinases. *Proteus mirabilis* has been increased extended-spectrum β-lactamase (ESBL) production. The most predominant enzymes of *Proteus mirabilis* such as TEM, CTX-M,VEB- and PER are less common (Miro *et al*.,2005).

Antibiotics resistance gene of Proteus mirabilis

Antibiotic resistance in human pathogens becomes a major problem in public health. Antibiotics resistance in the field of medical and agriculture is due to horizontal mobile genetic transfer elements that transmit more than one resistance genes (Shibata *et al*.,2003).

Plasmids, transposons, and integrons play important roles in transfer antibiotic resistance gene in bacterial species (Hansson *et al*.,2002). Antibiotic resistance of aminoglycosides, chloramphenicol, β-lactams, trimethoprim, erythromycin, and rifampin is due to integrons gene transfer (Patridge *et al*., 2002).

Proteus mirabilis is show resistant against ampicillin, tetracycline, gentamycin, and kanamycin. This resistance is occurred due to Class 1 integrons that carrier the antibiotic resistant genes, such as *aadA1, aadB,* and *aadA2*. Class 2 integrons also involved in transfer antibiotic resistance gene included: *dhfr1, sat1,* and *aadA1*.

The mutations in *gyrA* and *parC gene* of *Proteus mirabilis* show resistance against nalidixic acid. The resistant of ampicillin in *Proteus mirabilis* is due to *bla*TEM-1. and *bla*TEM-1, that were able to transmit resistance gene from *Proteus mirabilis* into *Escherichia coli* by conjugation (Shin-hee kim *et al*.,2005).

ESBL producer proteus mirabilis

The production of CBLs belonging (ACC, CMY/LAT and DHA) of *Proteus mirabilis* has been reported occasionally (Moland *et al.,* 2006). *Proteus mirabilis* producing ESBL has been identified in 1997 (Endimiani *et al*., 2005). This is the first strain of *P. mirabilis* that producing an acquired CBL (CMY-16) was identified in 2003 (Andrea *et al*., 2006).

Increase antibiotic resistance of *Proteus mirabilis* against third generation cephalosporins was observed in community and hospitalised patients.

Laboratory diagonosis of Proteus mirabilis

Proteus mirabilis can be identified by their robust swarming motility and urease production in clinical and microbiology laboratories. This Gram-negative *Proteus mirabilis* are motile, indole-negative, lactose-negative, and also have ablility to produces hydrogen sulfide (Hara *et al*., 2000).

Vaccine against Proteus mirabilis there is no commercially available vaccines is present against *Proteus mirabilis*. However, the vaccine of *P. mirabilis* are being tested in a murine model of ascending UTI (Habibi *et al*., 2015).

Conclusion

Proteus mirabilis is a pathogenic organism it caused number of infection in human. Their pathogenicity is promoted by number of virulence factors. Such as adhesins, flagella, toxins, quorum-sensing, enzymes and immune invasion This information about *Proteus* virulence will help to a better understanding of infectious processes and will allow to develop new effective procedure for prevention and clinical treatment.

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References

Alamuri P, Mobley HLT. 2008. A novel autotransporter of uropathogenic Proteus mirabilis is both a cytotoxin and an agglutinin. Molecular Microbiology **68,** 997–1017. http://dx.doi.org/10.1111/j.1365-2958.2008.06199.x

Andrea DMM, Nucleo E, Luzzaro F,Giani T, Migliavacca R, Vailati F, Kroumova V, Pagani L, Rossolini GM. 2006. CMY-16, a novel acquired AmpC-type b-lactamase of the CMY/LAT lineage in multifocal monophyletic isolates of Proteus mirabilis from Northern Italy.Antimicrob Agents Chemother **50,** 618–624.

Antoni RÓ, Agnieszka T, Magdalena M, Iwona k, Agnieszka M, kingaostrowska, Dominika D, Agnieszka Z, Agata P, Małgorzata S, Paweł S. 2012. *Proteus* sp. an opportunistic bacterial pathogen classification, swarming growth, clinical significance and virulence factors. Folia Biologica et Oecologica **8**, 1–17. http://dx.doi.org/10.2478/fobio-2013-0001.

Auwaerter P. 2008. Antibiotic guide. Johns Hopkins ABX (antibiotic) Guide, Baltimore, MD.

Bahrani FK, Mobley HL. 1994. Proteus mirabilis MR/P fimbrial operon: genetic organization, nucleotide sequence, and conditions for expression. Journal of Bacteriology **176,** 3412–3419.

Baldo C, Rocha SPD. 2014. Virulence factors of uropathogenic *Proteus mirabilis*. International Journal of Scientific and Technology Research **3(11),** 24-27.

Braun V, Focareta T. 1991.Pore-forming bacterial protein hemolysins (cytolosins). Critical Reviews in Microbiology **18,** 115–158. http://dx.doi.org/10.3109/10408419109113511

Christopher C, Carrie A, Poore Xin L, Harry LT, Mobley. 2000. Pathogenesis of *Proteus mirabilis* urinary tract infection. Microbes and Infection **2,** 1497–1505.

Coker C, Poore CA, X Li, Mobley HLT. 2000. Pathogenesis of Proteus mirabilis urinary tract infection. Microbes and Infection **2,** 1497–1505.

Endimiani A, Luzzaro F, Brigante G, Perilli M, Lombardi G, Amicosante G. 2005. *Proteus mirabilis* bloodstream infections risk factors and treatment outcome related to the expression of extended-spectrum β-lactamases. Antimicrob Agents Chemother **49,** 2598–2605. http://dx.doi.org/10.1128/AAC.49.7.2598-2605.2005

Habibi M, Asadi Karam MR, Shokrgozar MA, Oloomi M, Jafari A, Bouzari S. 2015. Intranasal immunization with fusion protein MrpH·FimH and MPL adjuvant confers protection against urinary tract infections caused by uropathogenic Escherichia coli and Proteus mirabilis. Molecular Immun **64,** 285-294. http://dx.doi.org/10.1016/j.molimm 2014.12.008

Hansson KL, Sundstro M, Pelletier A, Roy PH. 2002. Intl2 integron integrase in Tn7. Journal of Bacteriology **184,** 1712–1721.

Hara CM, Brenner FW, Miller JM. 2000. Classification, identification and clinical significance of *Proteus, Providencia and Morganella*. Clinical Microbiology Reviews **13,** 534-546.

Janda JM, Abbot SL. 2006. The Enterobacteriaceae. ASM Press. Washington. 233–259. http://dx.doi.org/10.4236/jss.2016.45025

Kaca W, Glenska J, Lechowicz L, Grabowski S, Brauner A, Kwinkowski M. 2011. Serotyping of

Proteus mirabilis Clinical Strains Based on Lipopolysaccharide O Polysaccharide and Core Oligosaccharide Structures. Published in Russian in Biokhimiya **76(7),** 1039-1050.

Knirel YA. 1999. Structure of the O-antigenic polysaccharides of *Proteus* bacteria. Polish Journal of Chemother **73,** 895–9071. http://dx.doi.org/10.1007/s00005-006-0031-1

Liaw SJ, Lai HC, Wang WB. 2004. Modulation of Swarming and Virulence by Fatty Acids through the RsbA Protein in *Proteus mirabilis* Infection and Immunity **72(12),** 6836–6845. http://dx.doi.org/10.1128/IAI.72.12.6836-6845.2004

Lukomski S, Serwecinska L, Rozalski A, Dziadek J, Staczek P, Jaworski A. 1991. Cell-free and cell-bound hemolytic activities of Proteus penneri determination by different Hly determinants. Canadian Journal of Microbiology. **37**, 419–424. http://dx.doi.org/10.1139/m91-068

Manos J, Belas R. 2006. The Genera *Proteus, Providencia,* and *Morganella*. Prokaryotes **6,** 245–269.

Matthews SJ, Lancaster JW. 2011. Urinary tract infections in the elderly population. American Journal of Geriatric Pharmacotherapy **9,** 286–309. http://dx.doi.org/10.1016/j.amjopharm 2011.07.002.

Miro E, Mirelis B, Navarro F, Alba R, Raúl JM, Carme R, Laura G, Pere C. 2005. Surveillance of extendedspectrum b-lactamases from clinical samples and faecal carriers in Barcelona, Spain. Journal of Antimicrobe Chemother **56,** 1152–1155. http://dx.doi.org/10.1093/jac/dki395.

Mobley HL, Chippendale GR, Swihart KG, Welch RA. 1991. Cytotoxicity of the HpmA hemolysin and urease of Proteus mirabilis and Proteus vulgaris against cultured human renal proximal tubular epithelial cells. Infection and Immunity **59,** 2036–2042.

Mobley HL, Belas R. 1995. Swarming and pathogenicity of Proteus mirabilis in the urinary tract. Trends Microbiol **3(7),** 280-284. http://dx.doi.org/10.1016/S0966-842X(00)88945-3

Moland ES, Hanson ND, Black JA, Hossain A, Song W, Thomson KS. 2006. Prevalence of newer β-lactamases in Gram-negative clinical isolates collected in the United States from 2001 to 2002. Journal of Clinical Microbiology **44,** 3318–24. http://dx.doi.org/10.1128/JCM.00756-06

Mutta RN, Oliveira MN, Magathaes PSF, Dias AM, Aragho LP, Forti AC, Carlvalho CBM. 2003. Plasmid mediated extended spectrum beta lactamase producing strain of enterobacteriaceae isolated from diabetic foot infections in Brazilian Diabetic center. Brazilian Journal of Infectious Diseases **7(2),** 129-134. http://dx.doi.org/10.1590/S141386702003000200006.

Nicholson EB, Concaugh EA, Mobley HL. 1991. Proteus mirabilis urease: use of a ureA-lacZ fusion demonstrates that induction is highly specific for urea. Infection and Immunity **59,** 3360–3365.

Nielubowicz, Greta R, Sara N, Smith, Harry LT, Mobley. 2008 Outer membrane antigens of the uropathogen Proteus mirabilis recognized by the humoral response during experimental murine urinary tract infection. Infection and Immunity. **76(9),** 4222-4231. http://dx.doi.org/10.1128/IAI.00533-08

Park YJ, Lee S, Kim YR. 2006. Occurence of extended-spectrum b-lactamases and plasmid-mediated AmpC b-lactamases among Korean isolates of Proteus mirabilis. Journal of Antimicrobal Chemother **57,** 156–158.

Parsek MR, Singh PK. 2003. Bacterial biofilms: An emerging link to disease pathogenesis. Annual

Review Microbiology **57,** 677. http://dx.doi.org/10.1146/annurev.micro.57.030502.090720.

Patridge SR, Collis CM, Hall RM. 2002. Class 1 integron containing a new gene cassette, *aadA10,* associated with Tn1404 from R151. Antimicrobe Agents Chemother **46,** 2400–2408. http://dx.doi.org/10.1128/AAC.46.8.2400-2408.2002

Pearson MM, Sebaihia M, Churcher C, Quail MA, Seshasayee AS, Luscombe NM, Abdellah Z, Arrosmith C, Atkin B, Chillingworth T, Hauser H, Jagels K, Moule S, Mungall K, Norbertczak H, Rabbinowitsch E, Walker D, Whithead S, Thomson NR, Rather PN, Parkhill J, Mobley HL. 2008. "Complete genome sequence of uropathogenic Proteus mirabilis, a master of both adherence and motility." Journal of Bacteriology **190(11),** 4027-4037. http://dx.doi.org/10.1128/JB.01981-07

Pellegrino R, Scavone P, Umpiérrez A, Maskell DJ, Zunino P. 2013. "Proteus mirabilis uroepithelial cell adhesin (UCA) fimbria plays a role in the colonization of the urinary tract. Pathogens and Disease **67,** 104-107. http://dx.doi.org/10.1111/2049-632X.12027

Phan H, Lehman D. 2012. Cerebral abscess complicating Proteus mirabilis meningitis in a newborn infant. Journal of Child Neurology **27(3),** 405-407. https://doi.org/10.1177/0883073811422271

Rocha SP, Pelayo JS, Elias WP. 2007. Fimbriae of uropathogenic Proteus mirabilis. FEMS Immunology and Medical Microbiology **51,** 1-7. http://dx.doi.org/10.1111/j.1574-695X.2007.00284.x

Sara MS. 2014. Importance of biofilms in urinary tract infections: New therapeutic approaches. Advance Human Biology, 1–13. http://dx.doi.org/10.1155/2014/543974.

Saurina G, Quale JM, Manikal VM, Oydna E, Landman D. 2000. Antimicrobial resistance in Enterobacteriaceae in Brooklyn, NY: epidemiology and relation to antibiotic usage patterns. Journal of Antimicrobal Chemother **45**, 895-898.

Shibata N, Doi Y, Yamane K, Yagi T, Kurokawa H, Shibayama K, Kato H, Kai K, Arakawa Y. 2003. PCR typing of genetic determinants for metallo-ß-lactamases and integrases carried by gram-negative bacteria isolated in Japan, with focus on the class 3integron. Journal of Clinical. Microbiology **41,** 5407–5413.

Shin-hee kim, cheng-i wei, haejung. 2005. an Molecular Characterization of Multidrug-Resistant Proteus mirabilis Isolates from Retail Meat Products. Journal of Food Protection **68(7),** 1408–1413. https://doi.org/10.4315/0362-028X-68.7.1408

Unhanand M, Mustafa MM, McCracken GH, Jr., Nelson JD. 1993. Gram-negative enteric bacillary meningitis: a twenty- one-year experience. Journal of Paediatrics **122(1),** 15-21. http://dx.doi.org/10.1136/fn.88.3.F173

Walker KE, Moghaddame SJ, Lockatell CV, Johnson D, Belas R. 1999. ZapA, the IgA-degrading metalloprotease of Proteus mirabilis, is a virulence factor expressed specifically in swarmer cells. Molecular Microbiology **32,** 825–836.

Yong D, Lim Y, Song W, Choi YS, Park DY, Lee H, Kim JM, Chong Y. 2005. Plasmid-mediated, inducible AmpC β-lactamase (DHA-1)-producing Enterobacteriaceae at a Korean hospital: wide dissemination in *Klebsiella pneumoniae* and *Klebsiella oxytoca* and emergence in *Proteus mirabilis*. Diagnostic Microbiology and Infectious Disease **53,** 65–70.

Zunino P, Geymonat L, Allen AG, Legnani CF, Maskell DJ. 2000. Virulence of a Proteus mirabilis

ATF isogenic mutant is not impaired in a mouse model of ascending urinary tract infection. FEMS Medical Microbiology and Immunology **29,** 137-143.