

compared to that of HepG2 or SNU475 with the GA or AA genotype.

Conclusions: Our findings suggested that the EGF 61AA genotype may lower HCC risk compared with GG and GA genotypes, and have lower level of EGF protein. In addition, block EGF signaling transduction via gefitinib can slowdown the proliferations of some HCC cell lines.

I-29 The natural history of infections caused by varicella-zoster virus (VZV): primary infection, transmission, latency, and reactivation.

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Studies of live attenuated varicella vaccine (Oka strain) have led to increased understanding of the behavior of this virus in human populations. For example, it has become clear that VZV spreads predominately from the skin lesions of patients with varicella (chickenpox) or zoster (shingles), which contain high concentrations of cell-free virions that are highly transmissible to others by the airborne route. At least 3 cellular receptors for VZV have been identified. This presentation will focus on the importance of the mannose 6-phosphate receptor (MPR) and its role in viral entry and egress from cells. Because MPRs are lost during the natural maturation of the superficial epidermis, VZV-infected maturing keratinocytes release infectious viral particles into the epidermal vesicles that form during varicella or zoster. In human infection, cellular immunity is required for host defense against VZV because non-epidermal cells express MPRs and thus do not release infectious virions. VZV thus spreads from one cell to another without entering the extracellular space. The exclusive cell-to-cell spread of VZV in the body contributes to the relatively long varicella incubation period, decreases the viral load during disease (because much of the intracellular virus is degraded in endosomes), and prevents the host from being overwhelmed by VZV. In evolutionary terms, it is an advantage for the virus not to overwhelm its host and to establish a latent infection so that it can persist after a varicella epidemic has exhausted the population of susceptible hosts, and reactivate to spread again, after a population of susceptible hosts is regenerated.

In an in vitro neuronal model of VZV infection, only cell-free VZV establishes latent infection. Because the epidermis is the only site in which infectious free virions emerge, this observation suggests that skin infection is necessary for the establishment of VZV latency. Infection of intraepidermal sensory nerve terminals enables VZV to establish latency in dorsal root and cranial nerve ganglia. During latency, a limited number of VZV genes are transcribed. The same genes are transcribed during latency in infected human ganglia and in cultured intestinal neurons isolated from either guinea pig or mouse. This neuronal model of VZV infection is useful because lytic or latent infections can be studied and VZV can be reactivated from latency. Both wild-type VZV and the vaccine (Oka) strain can establish latency and reactivate in neurons in vitro.

Basic studies on VZV have helped to promote understanding of how varicella vaccine behaves in human hosts. This knowledge, in turn, has contributed to recommendations for vaccine use. For example, the risk of manifesting zoster is low in vaccinees who lack a history of skin lesions from either vaccine or wild type VZV. In addition, skin lesions with infectious VZV are required for host-to-host transmission; therefore, decreasing the number of skin lesions due to VZV decreases VZV transmission. In order to maximize protection of vaccinees from chickenpox and minimize skin lesions, two

doses of vaccine are now recommended for all children in the United States.

Concurrent Session 5 – Usage of Antibiotics and MRSA

I-30 Antibiotics application in China

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Antimicrobial agents is the most frequent prescribed drug in China, near 40% of the drug consumption is antimicrobial agents, 60–70% of hospitalized patients receive antimicrobial agent therapy and 20–30% outpatient prescriptions contain those agents. The top three antimicrobials by the drug classification are fluoroquinolone, cephalosporin and macrolide. The irrational antibiotic application is a severe public health problem in China.

In community and hospital setting, antimicrobials are used for the treatment of bacterial infection, common cold and other un-infectives. The catalog of antimicrobials irrational use reasons includes prescription without indication, favoring intravenous administration, unnecessary combination, longer duration, higher dosage and others.

Except healthcare consumption, half of the antibiotic output is used in animal breeding as growth promoter, which is added in the animal feeding.

The reasons of irrational use are: healthcare system financial compensation defect, patient claim and pressure, unmet physician education, STG unavailable and industrial promotion.

The results of irrational use of antimicrobials are:

1. Severe bacterial resistance: 70% *E. coli* being resistant to fluoroquinolone, over 80% macrolide-resistant *Streptococcus* and *Staphylococcus* being detected, ESBLs(+) *Enterobacteriaceae* being 10–20%, penicillin non-sensitive *S. pneumoniae* increasing steadily, methicillin-resistant *Staphylococcus* being 60% national-widely, etc.
 2. Antibiotic-related ADR and drug sufferings: 50% ADR report collected in national ADR center was antibiotic-related, some national wide drug sufferings was reported occasionally.
 3. Wasting medicinal resource.
- The measures fighting against the antibiotic irrational use should be:
1. Healthcare system reform, which is being on the way.
 2. STG generating and enforcing; some hospitals or medical associations are preparing their own STG.
 3. Professional employees and patients education.
 4. Legalization industrial promotion.
 5. Restriction of animal use for growth promoter.

I-31 Prenyltransferases as targets for antibiotic drug discovery

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Prenyltransferases are involved in many biological pathways; thus they are useful for developing new drugs for various diseases. We have studied by structural analysis the product chain length determinants of several *trans*-type prenyltransferases, including geranylgeranyl pyrophosphate synthase (GGPPS) and so on. The specificities were determined by the size and depth of the activity site cavity. Large amino acids form the floor to block product further elongation. In addition, we solved the structures