PrP^{Sc} was found to be intracellular and most localized with ligands of the Golgi marker. In uninfected and cured M2B cells PrP^{C} was found at the plasma membrane. 2) Our data showed to differentiate PrP^{C} and PrP^{Sc} in high concentration GdnHCl treated M2B and cured M2B cells.

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P-057

The Role of Aberrant Nucleotide Guanine Derivatives in the Pathophysiology of Enteropathogenic and Enterohemorrhagic *Escherichia coli*

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Introduction: Aberrant Nucleotide guanine derivatives function as bacterial signal molecules that transduce various environmental signals outside a host such as starvation or stressful conditions into the cells and subsequently induce a global adaptive response. Among them, guanosine tetraphosphate (ppGpp) and cyclic diguanylate (c-di-GMP) are well-known as an alarmone that induces the stringent response and a universal second messenger in many bacterial species, respectively. In this study, the role of aberrant nucleotide guanine derivatives was examined in enterohemorrhagic *E. coli* (EHEC) and its protype strain, enteropathogenic *Escherichia coli* (EPEC), a major cause of infant diarrhea especially in developing countries.

Materials and Methods: To investigate the aberrant nucleotide guanine derivatives-dependent changes in both EHEC and EPEC, we created ppGpp-defective mutants of EHEC/EPEC by inactivating both *relA* and *spoT* genes known to encode ppGpp synthetase in addition to an arabinose inducible c-di-GMP synthetase (the *yddV* gene product)-over expressing strains of EHEC. We performed the proteomic and transcriptomic analyses, and examined the *in vivo* virulence of both wild type and mutant strains to compare their pathophysiological alterations.

Results: Our results demonstrated that the lack of ppGpp in EPEC (i) de-repressed the expression of the Type IV bundle forming pili, (ii) repressed the expression of LEE1, a key transcriptional activator of the LEE (locus of enterocyte and effacement) pathogenicity island, and (iii) lowered the transcription of the *gadAB* acid resistance system encoding glutamate decarboxylase. Supportingly, the whole genome-scale microarray analyses of the wild type and ppGpp null EHEC/EPEC mutant strains showed significant differences in several factors associated with transcriptional regulation, acid resistance and virulence/anti-virulence. In addition, we showed that over-expression of the *yddV* gene in EHEC resulted in a significant decrease in motility.

Conclusions: These results imply that the aberrant nucleotide guanine derivatives, especially ppGpp and c-di-GMP, involve in the pathophysiology of both EHEC and EPEC and contribute to bacterial infection during passage through the gastrointestinal tracts.

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P-058

Lactose Induces the Expression of Shiga toxins in Enterohemorrhagic *Escherichia coli* O157:H7

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Introduction: Enterohemorrhagic *Escherichia coli* (EHEC) O157:H7 causes serious diseases in humans and animals, including haemorrhagic colitis and haemolytic uremic syndrome. It is well known that the production of Shiga toxins (Stxs) by EHEC is one of the major virulence factors and has been used to detect EHEC from various food and environmental samples. In our attempt to identify novel Stx-inducing signals, we found that the EC medium, commonly used for selective enrichment of EHEC O157:H7, was able to induce the expression of Stxs. In this study, therefore, we investigated a Stx-inducing factor(s) present in the EC medium.

Materials and Methods: To identify the Stx-inducing signal(s) present in the EC medium, the expression of Stxs (Stx1 & 2) was analyzed in the absence or presence of each ingredients of the EC medium using quantitative real-time RT- PCR. The results were verified using Luria-Bertani (LB) medium with or without the Stx-inducing components identified in this study.

Results: A simple comparison of the nutrient and chemical composition in the EC medium with those in the other four commonly-used media (LB, trypticase soy broth, brain heart infusion broth, and buffered peptone water) revealed that the two unique components, bile salts and lactose, are present in the EC medium. The experimental analyses demonstrated