REVIEW ARTICLES

Cell cycle and cell signal transduction in marine phytoplankton*

LIU Jingwen[1,2], JIAO Nianzhi[2]** and CAI Huinong[1]

(1. Bioengineering School of Jimei University, Xiamen 361021, China; 2. State Key Laboratory of Marine Environmental Sciences of Xiamen University, Xiamen 361005, China)

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Abstract As unicellular phytoplankton, the growth of a marine phytoplankton population results directly from the completion of a cell cycle, therefore, cell-environment communication is an important way which involves signal transduction pathways to regulate cell cycle progression and contribute to growth, metabolism and primary production and respond to their surrounding environment in marine phytoplankton. Cyclin-CDK and CaM/Ca^{2+} are essentially key regulators in control of cell cycle and signal transduction pathway, which has important values on both basic research and applied biotechnology. This paper reviews progress made in this research field, which involves the identification and characterization of cyclins and cell signal transduction system, cell cycle-control mechanisms in marine phytoplankton cells, cell cycle proteins as a marker of a terminal event to estimate the growth rate of phytoplankton at the species level, cell cycle-dependent toxin production of toxic algae and cell cycle progression regulated by environmental factors.

Keywords: marine phytoplankton, cell cycle, cell signal transduction.

Studies on growth of phytoplankton in terms of individual cells require an understanding of the cell cycle. In unicellular phytoplankton, the completion of a cell cycle leads to growth of the population. The growth rate can then be estimated by monitoring the temporal changes in the percentage of the cells that traverse a phase of the cell cycle leading to mitosis. This method does not require incubation and is free from potential bottle effects. Furthermore, cell loss due to grazing, import or export, or death does not significantly affect growth rate estimation. In addition, the accuracy of the cell cycle method is presumed not to be affected by varying growth conditions. For example, proliferating cell nuclear antigen (PCNA) can be used to indicate whether a phytoplankton population is actively growing. Such application would be particularly useful in monitoring the initiation of a bloom. Prior to the emergence of the bloom, the cell concentration of a phytoplankton may be low, whereas the cells may be actively dividing. The low cell number and high division rate would be difficult to detect with traditional methods such as cell counts, due to potential effects of grazing or other removal processes. It can be easily detected by measuring the percentage of the cell population that contains high levels of the cell cycle proteins. Besides, the proteins will facilitate studies on how environmental factors affect the progression or arrest of the cell cycle. On the other hand, the regulation of cell cycle progression is a complicated process which involves kinase cascades, protease action, production of second messengers and other operations. Many environment stimuli have something to do with Ca^{2+} and calmodulin (CaM) in plants and animals. Ca^{2+}/CaM is a key component of the evolutionarily conserved signal transduction cascades and also is required for cell proliferation. These signal pathways occur widely in eukaryotes and are involved in regulation of a variety of cellular activities such as stress response and cell proliferation. The ubiquity and conservation of Ca^{2+}/CaM signal system suggest that it may exist in phytoplankton metabolism. Application of cell cycle, cell signal transduction and molecular techniques to marine ecosystem studies (especially harmful bloom caused by marine phytoplankton) and to explore the molecular mechanisms of environmental factors that affect cell proliferation in marine phytoplankton will be a very important and promising research.

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** To whom correspondence should be addressed; E-mail: jiao@xmu.edu.cn

1 Cell cycle

1.1 Cell cycle proteins

Studies on growth of phytoplankton in terms of individual cells require an understanding of the cell cycle. A complete cell cycle consists of the G_1 phase, the S phase, the G_2 phase, and the M phase. The cell cycle in phytoplankton is strictly regulated in the course of cell division, proliferation and growth. There are two major control points in the cell cycle, the G_1/S transition and the G_2/M transition, respectively. A family of cyclin-dependent kinases (CDKs), including $p34^{cdc2}$ and its analogous proteins and CDK inhibitors (CKI), is the central part of the cell cycle-control machinery[1]. Estimation of growth rate of phytoplankton at the species level is important for understanding how one species interacts with another, or with the environment, and how blooms arise and decline. A cell has to complete its growth cycle, typically consisting of G_1, S, G_2, and M phases for eukaryotes, before it divides to produce two daughter cells. The population size is dependent of the rate of cell division and the tare of cell removal due to grazing, export, and infection of bacteria or virus. Therefore cell cycle protein, as a cell cycle marker would be useful in calculating cell division rate and the growth of phytoplankton population. This method does not require incubation and is free from potential bottle effects[2,3]. Among the increasing number of cell cycle-dependent proteins, PCNA, $p34^{cdc2}$, and cyclin B are very conserved ones across a wide phylogenetic range. These cell cycle proteins are good candidates for such a cell cycle marker, because they are cell-cycle-dependent in synthesis and abundance; they are ubiquitous in the phylogenetic spectrum; and they are highly conserved during the evolutionary process.

1.1.1 Proliferating cell nuclear antigen (PCNA)

PCNA is an auxiliary protein to DNA polymerase δ and ε and is essential for DNA synthesis. It is a highly conserved protein in both amino acid sequence and biochemical function. The synthesis level and abundance of PCNA dramatically increase in the early S phase of the cell cycle and can thus be a useful marker for the estimation of growth rate at the species level via the cell cycle approach[4]. A PCNA gene fragment was isolated by reverse transcription-PCR from the marine unicellular alge *Tetraselmis chui* Butcher (Prasinophyceae), which is 616 bp in length and contains an open reading frame of 205 amino acids. The deduced amino acid sequence shows 80% and 88% similarities to human and rice PCNA, respectively[5]. The gene encoding PCNA has been isolated from the marine coccolithophorid microalga *Pleurochrysis carterae* (Braarud et Fagerland) (Christensen) (Haptophyceae). Two mRNAs (Pcpcna 1 and Pcpcna 2) were identified and they contain an common identical coding region of 222 amino acid residues and an untranslated sequence of 302 base pair (Ut1) and 246 base pair (Ut2), respectively. Pcpcna was found to be highly transcribed and translated during the exponential growth phase relative to the stationary growth phase, with a positive correlation between gene expression and growth rate[6]. Recently, PCNA was detected in *Prorocentrum donghaiense* Lu by enhanced chemiluminescence techniques with a monoclonal antibody. The observed band detected on Western blots of *P. donghaiense* had a molecular weight of 36 kD[7]. It is interesting that a PCNA-like protein in *P. donghaiense* close to 36 kD was also found in dinoflagellates *P. minimum* and *H. triquetra*[2] rather than the 55 kD protein reported in *C. cohnii* and *G. catenatum*[8]. The abundance of PCNA proteins was growth stage dependent and showed a cell cycle specific expression pattern with the highest expression in S phase and little expression in G_1 and G_2/M phases[7]. It is well known that dinoflagellates have an unusual chromosomal structure and the different size of the PCNA-like protein observed could be related to this variety in dinoflagellate chromosomal structure. It has been shown that dinoflagellates contain extensive stretches of Z-DNA[8] and the *C. cohnii* PCNA could have a different structure and size to properly interact with the large amounts of Z-DNA[9]. It is also important to note that dinoflagellates are a transition group from prokaryotic to eukaryotic evolution and they are a very diverse group. It has been suggested that early lineages of dinoflagellates may still possess a PCNA protein that has an apparent molecular size similar to other eukaryotic groups[10].

1.1.2 Cell cycle proteins (cyclins), cyclin-dependent kinases (CDKs) and the two points serve as the checkpoints

The cyclin B- and $p34^{cdc2}$-like proteins have been identified in marine phytoplankton so far[11]. Cyclin B shows a highest expression in G_2 and M phases, so it can be a useful cell marker for growth rate studies

on marine phytoplankton (esp. on harmful algal blooms)[12—14]. A gene fragment corresponding to cyclin box has been cloned from brown tide alga *Aureococcus anophagefferens*[12]. This algal gene fragment, designated as *Btcycl 1*, is quite similar to cyclin B. Based on the deduced amino acid sequence the oligopeptides were synthesized and used to raise an antiserum that detected on Western blots a protein of about 63 kD, the same size as cylin B in other organisms. So the *Btcycl 1* sequence and the antiserum will provide useful tools for studies on regulation of *in situ* growth rate for this brown tide alga.

It has been reported that a CDK-like protein kinase is present in the dinoflagellate *Crypthecodinium cohnii*[15]. Cell division in the dinoflagellate *Gambierdiscus toxicus* is phased to the diurnal cycle and accompanied by activation of the cell cycle regulatory protein, CDC2 kinase[16]. To understand the genetic control of algal cell division cycle that pertains to phytoplankton bloom dynamics in the sea, a gene coding for a cyclin-dependent kinase (CDK) for the chlorophyte *Dunaliella tertiolecta* has been cloned and analyzed[17]. The cDNA cloned, 1061 bp long, contained an open reading frame of 314 amino acids. FASTA and GAP analyses showed that this sequence was most homologous to cdc2 out of all known cdks, with an identity of 54%—68% and a similarity of 65%—76% to cdc2 in higher plants, animals, and yeast. Several signature domains of cdc2 were identified from this sequence, although the PSTAIRE and GDSEID motifs were replaced by PSTTLRE and GDCELQ, respectively. The $p34^{cdc2}$- and cyclin B-like proteins have been detected in *Dunaliella tertiolecta* (Chlorophyceae), with an apparent molecular mass 34 and 63 kD, respectively[14]. The two proteins decreased from the exponential to the stationary growth phase and their abundance only changed slightly during the whole cell cycle.

Several studies have suggested that thresholds of cyclin abundance may coordinate the cell growth and division cycles[18]. They thus imply that a delay in cell cycle progression due to nutrient limitation may be related to delay in build-up of cyclins. Therefore, $p34^{cdc2}$ and cyclin B are the cell cycle markers that are highly desirable for studies of environmental effects on phytoplankton, and for growth rate estimation.

1.2 Advantages and disadvantages by using cell cycle proteins as a marker to estimate growth rate of phytoplankton at the species level

The causes of marine phytoplankton are still elusive, largely because no information on its *in situ* growth rate is available. The poor knowledge of *in situ* growth rate is due to the lack of a proper method. Earlier studies have attempted to attribute formation and demise of the blooms to metereological and hydrographical events, fluctuation in groundwater flow, organic and micro nutrients, grazing, and virus infection. These factors are compounded in nature, while information on species-species growth rate of marine phytoplankton is very important for understanding the dynamics of marine phytoplankton populations and communities, such information is relatively limited due to the difficulty in measuring rates. A variety of approaches have been developed in the past, each with its own limitations[13]. By immunohistochemical and immunofluorescence methods, it was observed that the PCNA in *Dunaliella tertiolecta Butcher* (Chlorophyceae) was exclusively located in the nucleus and its abundance varied, being the highest in S-phase cells, lower in others, and undetectable in early G_1 or late M phase cells[19]. Synchronized cells of *P. donghaiense* Lu also showed a cell cycle specific expression pattern with the highest expression in S phase and little expression in the G_1 and G_2/M phases[7]. PCNA can be a good cell cycle marker for growth rate estimation by the cell cycle approach, because its cell cycle dependence has been established. The first growth rate model of this type was based on the measurement of frequency of dividing cells in the population[20]:

$$\mu = (1/nT_d)\sum_{i=1}^{n}\ln(1+f_i), \qquad (1)$$

where μ is growth rate (d^{-1}); n the number of samples collected within a day; T_d the duration of the cell division; and f_i the fraction of cells undergoing cell division in the ith sample. A limitation of this model is that the duration of cell division is usually short and that it is often difficult to monitor the frequency of dividing cells with reasonable sampling frequencies.

The PCNA-stained phase instead of the mitosis phase is considered as a "terminal" event, therefore the growth rate equation becomes[19]:

$$\mu = (1/nT_s)\sum_{i=1}^{n}\ln(1+f_i), \qquad (2)$$

where μ is growth rate (d^{-1}); n the number of samples taken within a 24 h period; T_s the duration of the PCNA-stained phase; and f_i the fraction of cell population that is PCNA-stained in the ith sample.

Until recently, little is known regarding marine phytoplankton PCNAs, although homologs of some of these proteins were detected in a few marine phytoplankton species. Its application to growth studies has been hampered largely by a scarcity of comparative information and appropriate probes for the genetically diverse phytoplankton.

With the recent evidence of significantly decreasing concentrations of ozone in the stratosphere and the concomitant increase in ultraviolet B radiation (UVB) for north and south temperate latitudes, many studies have stressed the effects of UV on marine phytoplankton and primary production[21,22]. In marine environments, UV radiation routinely causes DNA damage to phytoplankton cells, and the existence of DNA repair mechanisms has been demonstrated. However, it is still unclear how PCNA and DNA polymerase α participate in DNA repair in unicellular algae. Obviously, the value of using these proteins as growth indicators may decrease if their expression levels increase during DNA repair. Treating marine diatom, *Skeletonema costatum* (Greville) Cleve with UVC radiation for 15 min caused severe mortality during the 24 h period after treatment and the mRNA levels of PCNA increased by as much as 23 pmol · (g total RNA)$^{-1}$, compared with the control experiments. In contrast, massive cell deaths did not occur in cultures receiving UVA/B radiation, and UVA/B did not enhance the expression levels of PCNA. Based on the calculation of biologically effective UV doses, daily exposure to sunlight may increase the expression of PCNA genes in *S. costatum* by 12% at sea surface. This level of increase does not seriously affect the value of using these genes as growth indicators[23]. However, marine phytoplankton has varying sensitivities to UVB. UV radiation caused clearly damage to the cells of *Prorocentrum Donghaiense* Lu and increased the expression of PCNA protein to a certain extent. Thus dinoflagellate *P. Donghaiense* appears to be highly susceptible to UVB (315 nm, 1150 μW · cm^{-2}) exposure (unpublished), which could be related to the variety of dinoflagellate chromosomal structures. It is also important to note that dinoflagellates are a transition group from prokaryotic to eukaryotic evolution and they are a very diverse group. The role of UV on marine bacteria and viruses has been investigated in recent years, providing evidence that UVB may be more damaging to bacterial and viruses DNA compared to that of eukaryotic plankton, and protein synthesis in prokaryotic cells appears sensitive to UVB[24]. Dinoflagellates are intermediate between prokaryotic and eukaryotic and are noted for having many prokaryotic features. It is speculated that dinoflagellates—the special groups in evolution—may be much more sensitive to UVB radiation than any other phytoplankton. UVB-induced expressions in PCNA are likely to be more to a certain extent in coastal and oceanic waters and this level of increase more or less may affect the values of using PCNA protein or genes as a growth indicator for marine phytoplankton. Therefore, caution is needed in the application of these proteins or genes to all phytoplankton especially some species sensitive to UV radiation.

1.3 Cell cycle and toxin production in marine phytoplankton

It is generally known that the toxin production of toxic algae is affected by environmental and nutritional factors such as temperature, salinity, pH and nutrient supply. Moreover, the toxin production of toxic algae and its possible relation to cell cycle progression has received increasing attention in recent years. It is important to understand the mechanisms by which cell cycle controls the marine phytoplankton toxin synthesis. It is reported that toxin production and the toxin cell quota (Q_t) coupled to the G_1 phase of the cell cycle in *Alexandrium fundyense* Balech[25]. Analysis of toxin composition showed that PSP toxin content was always directly correlated to the duration of the G_1 phase[26]. Profiles of diarrhetic shellfish poisoning (DSP) toxins produced throughout the growth cycle and the cell cycle of the toxigenic marine dinoflagellate *Prorocentrum lima* were studied in triplicate unialgal batch cultures. DTX4 synthesis is initiated in the G1 phase of the cell cycle and persists into S phase ("morning" of the photoperiod), whereas DTX1 production occurs later during S and G_2 phases ("afternoon"). The evidence indicates that toxin synthesis is restricted to the light period and is coupled to cell cycle events[27]. The effects of environmental and nutritional factors on population dynamics and toxin production were examined in *Alexandrium catenella*. It showed that toxin content per cell was the highest in cell populations in the early exponential phase. Toxin content in the dinoflagellate reached its maximum during the S-phase of the cell cycle[28]. Erik et al.[29] reported that the light-dependent effect on toxicity and relationship to discrete phases of the cell cycle in a prymnesiophyte.

The coupling of toxicity expression with cell-cycle phases was studied in the toxic marine prymnesiophyte *Chrysochromulina polylepis*. Cell synchronisation of cultures in exponential or early stationary growth phases under nutrient-replete conditions was achieved by manipulation of the photoperiod. Toxicity expression, measured by the erythrocyte lysis assay (ELA), exhibited a dramatic drop in LC_{50} values (increase in toxicity) during the light period, although this effect was less pronounced after the first two generations of cell division when the cultures had entered the stationary phase. Similarly, haemolytic activity per unit cell volume decreased by a factor of 3 to 4 during the dark period over the first 48 hours, but became irregular towards the end of the experiment. Recently, the correlation between the content of three microcystins (types LR, RR and YR) and the cell cycle of an axenic strain of *Microcystis viridis*, NIES-102, was investigated . Microcystin concentration showed a positive linear correlation with DNA concentration. The microcystin content of the cells changed remarkably as the cell cycle proceeded, with maximum content in the G_2/M phase and minimum content in the G_0/G_1 phase[30].

1.4 Effect of environmental factors on phytoplankton cell cycle

The cell cycle in phytoplankton is strictly regulated in the course of cell division and is influenced significantly by environmental factors as well, such as light, temperature, nutrient supply and the interaction with virus. Jacquet et al.[31] studied the effect of light on the synchronization of cell cycling in several strains of the oceanic photosynthetic prokaryote *Prochlorococcus* using flow cytometry and suggested a close coupling between irradiance levels and cell cycling in *Prochlorococcus* spp. This study showed that complete darkness arrested most of the cells in the G1 phase of the cell cycle, and that light was required to trigger the initiation of DNA replication and cell division. Using light/dark synchronized cultures to monitor cell cycle responses, the *C. fusiformis* nitrate transporter *NAT* (NitrAte Transporter) mRNA levels were high in early G_1 phase, decreased through the remainder of G_1, then increased during DNA synthesis in S phase and into G_2, and finally decreased after M phase[32]. Claquin et al.[33] studied the elemental composition and the cell cycle stages of the marine diatom *Thalassiosira pseudonana* Hasle and Heimdal in continuous cultures over a range of different light-(E), nitrogen-(N), and phosphorus-(P) limited growth rates. Under all of the growth conditions, the decrease in the growth rate was linked with a higher relative contribution of the G_2 + M phase. The other phases of the cell cycle, G_1 and S, showed different patterns, depending on the type of limitation. All experiments showed a highly significant increase in the amount of biogenic silica per cell and per cell surface with decreasing growth rates. At low growth rates, the G_2 + M elongation allowed an increase of the silicification of the cells. This pattern could be explained by the major uptake of silicon during the G_2 + M phase and by the independence of this process on the requirements of the other elements. Thyrhaug et al.[34] investigated virus production in marine phytoplankton species and the relation of virus production with the host's cell cycle. In the experiment, *Pyraminonas orientalis*, growing synchronously in batch culture, was infected with its virus PoV(*pyramimonas orientalis* virus) at four different stages of the cell cycle and both the production of phytoplankton *Pyraminonas orientalis* and free virus depended on the time of infection. The difference in virus production may be attributed to light or cell cycle dependent regulation of host infection, metabolism, or burst size. At least, three hypotheses may explain the variation in virus production in *Pyraminonas orientalis*: (1) light- or cell cycle-dependent virus absorption and penetration, (2) cell cycle-dependent initiation of virus replication, and (3) variation in burst size. Viral activity is thought to be important in maintaining the diversity of phytoplankton communities. Regardless of the mechanism, these differences may be related to differences in the ecological strategies of the host and their ability to form blooms. Thus, viral activity depends on, in addition to nutrient availability, light conditions, vertical mixing, grazing pressure, and so on. One of the factors may affect the onset, development and termination of phytoplankton bloom.

2 Cell signal transduction in marine phytoplankton

Many environment stimuli have something to do with Ca^{2+} and calmodulin (CaM) in plants and animals. Ca^{2+} signal system is a very important transduction pathway, and CaM is the most important known receptor of intracellular Ca^{2+}, which is involved in regulation of many physiological activities. Ca^{2+}/CaM-dependent protein kinase (CaMK) is a u-

biquitous multifunctional enzyme. It requires Ca^{2+}-bound CaM for its activation, and its activity is involved in many cellular events. Increasing evidence now compellingly suggests that changes in the intracellular Ca^{2+} concentration may have a crucial role. In addition, the status of the intracellular calcium pools is critical for normal traverse of the cell cycle.

It has been shown that intracellular Ca^{2+} and IP (inositol 1, 4, 5-trisphosphate), two crucial messengers of the phospholipase C-regulated signal transduction pathways, may be involved in the encystment response of the dinoflagellates *Alexandrin catenella* and *Crypthecodinum cohnii*[35]. This encystment process can be induced by indoleamines such as melatonin and 5-methoxytryptamine under environmental stress, in which intracellular acidification is a pivotal step in committing the dinoflagellate to encystment. Thus, it has been proposed that melatonin-induced encystment is due to the metabolism of melatonin to 5-methoxytryptamine, which then stimulates a V-type H^+-ATPase on the acid vacuole. As a result of acidification of the intracellular pH, encystment ensues. This is the first demonstration of the possible involvement of Ca^{2+} and inositol phosphates as second messengers in dinoflagellates.

Lam et al.[36] studied the level of intracellular cAMP during the cell cycle of *Crypthecodinum cohnii*. cAMP peaked during the G_1 phase and decreased to a minimum during S phase. Similarly, cAMP-dependent protein kinase (PKA) activities peaked at both G_1 and G_2 + M phases of the cell cycle, decreasing to a minimum at S phase.

Recently, a full-length cDNA (1434 bp) of mitogen-activated protein kinase (MAPK), a key molecule of a signal transduction cascade, was isolated from the estuarine heterotrophic dinoflagellate *Pfiesteria piscicida*[37]. This cDNA (*Ppmapk1*) encoded a protein (PpMAPK1) of 428 amino acid residues that shared about 30%—40% amino acid similarity with MAPKs in other organisms. *Ppmapk1* expression level was correlated with growth rate, suggesting involvement of this gene in the regulation of cell proliferation.

More recently, our laboratory started investigating the Ca^{2+}/CaM in marine phytoplankton. CaM protein has been isolated and purified by chromatography-sepharose CL-4B from *Prorocentrum Donghaiense* Lu and the anti-CaM serum has also been developed. The strong single band detected on Western blots had a molecular weight of 16 kD (unpublished). Based on the above work, we first discovered that the effect of different N:P ratios of nutrient supply on the growth of *P. Donghaiense* Lu involved the Ca^{2+}/CaM signal transduction pathway. We found that intracellular Ca^{2+} concentration decreased dramatically when *P. Donghaiense* was cultured in a higher N:P nutrient supply while the concentrations of Ca^{2+}, CaM and cell cycle protein kinase p34cdc2 increased rapidly when the cells were treated with sufficient phosphate (unpublished). These results suggested that Ca^{2+}/CaM signal pathway might be involved in the regulation of marine phytoplankton interaction with the environment and might play an important role in regulating cell-cell communication. Further studies are required to investigate spatio-temporal variety of Ca^{2+} signals and examine the presence of Ca^{2+}/CaM signal transduction cascades response in modulating the interaction between phytoplankton cell proliferating and environmental factors, such as Ca^{2+}-dependent protein kinase, phosphatases, PLC, CaM-binding protein, activated GTP-binding protein (G-protein) and Ca^{2+} channel. These studies will shed light on the understanding of the relationships between growth, cell cycle, cell signal transduction, bloom formation and the biogeochemical role of marine phytoplankton.

3 Perspectives for the research on cell cycle and cell signal transduction in marine phytoplankton

Molecular biological techniques are useful tools for addressing some important questions for marine phytoplankton. Since the last decade the study of cell cycle and cell signal transduction has progressed much faster and detailed in plants and animals. However, the application of theses techniques in this field is rather scattered and no well-established procedures are available. For marine phytoplankton, studies on their transduction pathways, mechanisms and their functions in regulating cell growth and relationships with environmental factors are just starting. The major issues we are focusing on at present are (1) to identify new members in cell cycle progression and dissect the cell cycle control, checkpoint mechanisms by which marine phytoplankton interacts with the environment and changes it growth states; (2) the probes and antisera development of the proliferation and cell division cycle-related genes and proteins will provide

useful tools for studies on regulation of *in situ* growth rate for marine phytoplankton; (3) calcium and its ubiquitous intracellular receptor CaM are required for cell proliferation. Studies in a variety of model systems are quite important for identifying components of the Ca^{2+}/CaM cascade required for movement of quiescent cells into the cell cycle as well as for proliferating cells to move from G_1 to S, G_2 to M and through mitosis; (4) global warming and increased UV radiation are occurring, yet their effects on the world's largest ecosystem, the marine pelagic realm, are largely unknown. These environmental signal factors also made a great impact on marine ecosystem at different organizational and functional levels. Which signal transduction pathways (such as Ca^{2+}/CaM) are involved in heat shock reaction or light signal pathway in marine phytoplankton are still unknown. It is interesting to study the interaction between environment and phytoplankton from the view of cell cycle and cell signal transduction; (5) to study the probable signal transduction pathway of environment stimulation in viruses-phytoplankton. Regulate production of viruses and phytoplankton, then affect the onset, development and termination of phytoplankton blooms; (6) It is noteworthy that cell cycle and Ca^{2+}/CaM signal system will help us not only to understand the complex interaction between organisms, substance and energy in marine ecosystem; but the potential regulation attributed to environmental information transduction-dependent regulation of marine ecosystem balance.

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