| Sr. No. | Cell cycle Proteins     | Functions  |
|---------|-------------------------|--|
|         |                         | /S transition  |
| 1       | CDKF                    | It activates CDKD  |
| 2       | СДКД                    | CDKD activates CDKA/CYCD complex, which  |
|         |                         | inturn phosphorylates RB protein   |
| 3       | CYCD                    | It functions as a substrate for CDKA. It binds                                   |
|         |                         | with CDKA and forms CDKA/CYCD complex  |
| 4       | СДКА                    | It is an enzyme which forms complex with CYCD                                    |
|         |                         | and phosphorylates RB protein  |
| 5       | Retinoblastoma (RB)     | Hyperphosphorylated RB protein inhibits  |
|         |                         | binding of transcription factors (E2F) and the                                   |
|         |                         | docking protein (DP)   |
| 6       | E2FA                    | Its accumulation stimulates cell cycle   |
|         |                         | progression towards S phase  |
| 7       | E2FC                    | Its accumulation represses the expression of S                                   |
|         |                         | phase genes  |
| 8       | ICK1                    | It controls the activity of CDKA/CYCD  |
|         |                         | complex. Up-regulation of ICK1expression   |
|         |                         | down-regulates CDKA activity   |
|         | -                       | M transition   |
| 1       | Wee1                    | It maintains Tyr15 residue of CDKA in  |
|         |                         | phosphorylated state. This inhibits progress of                                  |
| 2       | DAS2                    | cell cycle towards M phase   |
| 2       | PAS2                    | It removes inhibitory phosphate from<br>CDKA/CYCB complex by antiphosphorylation |
|         |                         | process and allows entry of cell cycle from G2                                   |
|         |                         | to M phase   |
| 3       | СДКА                    | It is an enzyme which forms complex with CYCB                                    |
|         |                         | and gives signal to CDKB/CYCB complex to   |
|         |                         | initiate mitosis   |
| 4       | СҮСВ                    | It functions as a substrate for CDKA. It binds                                   |
| '       |                         | with CDKA and forms CDKA/CYCB complex  |
| 5       | CAKs (CDKF and CDKD)    | It activates CDKA/CYCB complex   |
| 6       | CDKB                    | It is a mitosis inducing factor  |
| 7       | E2FB                    | It binds with CDKB/CYCB complex and drives                                       |
| ,       |                         | cell cycle towards mitosis   |
| 8       | APC                     | It regulates ubiquitination and proteolysis of                                   |
| 0       |                         | CYCB   |
| 9       | CDC20                   | It activates APC/C during metaphase  |
| 10      | CDH1                    | It activates APC/C for the exit of mitosis                                       |
| 10      | MAD2 (Mitotic arrest    | They binds with CDC20 to activate APC/C  |
| **      | deficient 2) and BUBR1  |  |
|         | (Budding uninhibited by |  |
|         | benzimidazole R1)       |  |
| 12      | securin                 | Degradation of securin is required for anaphase                                  |
|         |                         | onset and activate separase enzyme.  |
|         |                         | Degradation of securins is important in the                                      |
|         |                         | spindle assembly checkpoint to ensure balanced                                   |

|                   |  | chromosome segregation and to avoid   |  |  |
|-------------------|--|---|--|--|
| 12                |  | aneuploidy  |  |  |
| 13                | Separase                                   | Activated separase enzyme cleaves the   |  |  |
|                   |  | cohesion complexes, thereby allowing sister chromatid separation  |  |  |
| 14                | СҮСВ                                       | It is a substrate required for phosphorylation of   |  |  |
| 14                | CIEB                                       | CDKB  |  |  |
|                   | СДКВ                                       | It interacts with CYCB and activates protein and  |  |  |
|                   |  | expression of genes required for cytokinesis  |  |  |
| 15                | APC/CCDC20 and                             | It mediates CYCB degradation. CYCB  |  |  |
|                   | APC/CCDH1                                  | proteolysis is required to inhibit CDKB activity  |  |  |
|                   |  | and to induce different cell processes such as  |  |  |
|                   |  | sister chromatid separation, disassembly of the   |  |  |
|                   |  | mitotic spindle, chromosome decondensation,   |  |  |
|                   |  | cytokinesis and reformation of the nuclear  |  |  |
|                   |  | envelope  |  |  |
| Endoreduplication |  |   |  |  |
| 1                 | ICK2                                       | It inhibits the activity of CDKA and CDKB   |  |  |
| 2                 | CDKB                                       | It is a mitotic inducing factor. Decrease in its  |  |  |
|                   |  | activity stimulates S-phase reentry, resulting in   |  |  |
| 2                 |  | diversion of cell cycle towards endocycle   |  |  |
| 3                 | CDKA                                       | It is an enzyme which forms complex with CYCB   |  |  |
|                   |  | and gives signal to CDKB/CYCB complex to<br>initiate mitosis  |  |  |
| 4                 | E2FB                                       |   |  |  |
| 4                 | EZFB                                       | It binds with CDKB/CYCB complex and drives cell cycle towards mitosis. Destruction of E2FB  |  |  |
|                   |  | transcription factor in the G2 phase leads to the   |  |  |
|                   |  | period of low CDKB activity. It blocks cell   |  |  |
|                   |  | cycle in S-phase, coupled with attenuation of   |  |  |
|                   |  | endocycle progression   |  |  |
| 5                 | Cul4Cdt2 E3 ubiquitin                      | It targets E2FB for destruction   |  |  |
|                   | ligase                                     |   |  |  |
| 6                 | E2FA                                       | E2FA during G1 phase drives CycE  |  |  |
|                   |  | transcription, which activates CDKA and   |  |  |
|                   |  | triggers entry into S phase and the subsequent  |  |  |
|                   |  | destruction and inactivation of E2Fc by RUB-  |  |  |
| _                 | EQE  | Cullin pathway  |  |  |
| 7                 | E2Fc                                       | Its accumulation represses the expression of S  |  |  |
|                   |  | phase genes. It inhibits cell division leading to enlarged cells  |  |  |
|                   | RUB-CUI                                    | LIN signaling pathway   |  |  |
| 1                 | CUL1                                       | It is a cell cycle regulating enzyme  |  |  |
|                   |  |   |  |  |
|                   |  |   |  |  |
| 3                 | CAND1                                      |   |  |  |
| 4                 |  |   |  |  |
|                   |  | formation of SCF E3 ligase complex  |  |  |
| 5                 | TIR1                                       |   |  |  |
| 6                 | ASK1 and Atcul1                            | They both binds with TIR1 to form ubiquitin   |  |  |
| 2<br>3<br>4<br>5  | RUB1/NEDD8   CAND1   SKP1 and F-box   TIR1 | It regulates CUL1 protein through neddylation<br>activating and conjugating enzymesan inhibitor of SCFThey binds with CUL1 protein and allows the<br>formation of SCF E3 ligase complexIt is an important protein for auxin signaling |  |  |

|    |                      | ligase complex (SCF <sub>TIR1</sub> )                            |
|----|----------------------|--|
| 7  | SCF <sub>TIR1</sub>  | This functions only in the presence of auxin. It                 |
|    |                      | starts degradation of E2FC protein with the help                 |
|    |                      | of COP9 signalsome and allows cell cycle to                      |
|    |                      | enter S phase  |
| 8  | Aux/IAA              | It acts as substrate for SCF <sub>TIR1</sub> . It interacts with |
|    |                      | SCF <sub>TIR1</sub> by direct binding with TIR1                  |
| 9  | COP9 signalsome      | an evolutionary conserved multiprotein complex                   |
|    | _                    | that has function in neddylation of CUL1                         |
|    |                      | protein in order to allow cell cycle to enter in S               |
|    |                      | phase  |
| 10 | SCF <sup>SKP2A</sup> | It degrades docking protein (DP) and helps in                    |
|    |                      | progress of S phase  |