

Table S3. Table of kinetic rate constants used in model with references.

| Rate Constant | Value   | Reaction  | Source                 |
|---------------|---------|---|------------------------|
| kass_rea      | 0.001   | Production of ROS   | Experimental Data      |
| kass_reb      | 0.15    | Induction of a Simple DSB                                     | Experimental Data, [1] |
| kass_rec      | 0.03    | Degradation of ROS  | Experimental Data      |
| kass_red      | 0.6     | Recruitment of Ku70/80 to sDSB                                | [2]                    |
| kass_ree      | 0.02    | Ku70/80 leaving site of Damage                                | Model constant         |
| kass_ref      | 5e-006  | Ku70/80 binding to sDSB                                       | [3]                    |
| kass_reg      | 0.5     | Ku70/80 dissociation from sDSB                                | [3]                    |
| kass_reh      | 0.6     | Recruitment of DNA-PKcs to sDSB                               | [4]                    |
| kass_rei      | 0.02    | DNA-PKcs leaving site of Damage                               | Model constant         |
| kass_rej      | 9e-005  | DNA-PKcs binding to Ku70/80-sDSB Complex                      | [4]                    |
| kass_rek      | 0.3     | DNA-PK Autophosphorylation                                    | [4]                    |
| kass_rel      | 0.001   | Recruitment of LiIV/XRCC4 to sDSB                             | [5]                    |
| kass_rem      | 0.2     | LiIV/XRCC4 leaving site of Damage                             | Model constant         |
| kass_ren      | 0.00035 | LiIV/XRCC4 binding to DNA-PK-sDSB Complex                     | [5]                    |
| kass_reo      | 0.075   | Ligation of sDSB and dismantling of Repair Complex            | [5]                    |
| kass_rep      | 0.15    | Induction of a Complex DSB                                    | Experimental Data, [1] |
| kass_req      | 0.6     | Recruitment of Ku70/80 to cDSB                                | [2,6]                  |
| kass_rer      | 4e-006  | Ku70/80 binding to cDSB                                       | [3,6]                  |
| kass_res      | 0.4     | Ku70/80 dissociation from cDSB                                | [3]                    |
| kass_ret      | 0.6     | Recruitment of DNA-PKcs to cDSB                               | [4,6]                  |
| kass_reu      | 7e-005  | DNA-PKcs binding to Ku70/80-cDSB Complex                      | [4,6]                  |
| kass_rev      | 0.3     | DNA-PK Autophosphorylation                                    | [4,6]                  |
| kass_rew      | 0.001   | Recruitment of LiIV/XRCC4 to cDSB                             | [5]                    |
| kass_rex      | 0.0002  | LiIV/XRCC4 binding to DNA-PK-cDSB Complex                     | [5,6]                  |
| kass_rey      | 0.075   | Ligation of cDSB and dismantling of Repair Complex            | [5,6]                  |
| kMRN          | 0.75    | Activation and Binding of ATM and MRN                         | [7,8]                  |
| kass_rez      | 0.5     | H2AX Phosphorylation  | [9]                    |
| kass_reaa     | 0.5     | H2AX Phosphorylation  | [9]                    |
| kass_reab     | 0.5     | H2AX Phosphorylation  | [9]                    |
| kass_reac     | 0.5     | Damage Focus Formation  | [10]                   |
| kass_read     | 0.1     | Damage Focus Dismantling                                      | [10]                   |
| kass_reae     | 0.5     | ATM-MRN Complex binding to Damage Focus                       | [11]                   |
| kass_reaf     | 0.03    | ATM-MRN-Damage Focus Dismantling                              | [11]                   |
| kass_reaq     | 0.6     | Recruitment of PARP to sDSB                                   | [3]                    |
| kass_rear     | 0.02    | PARP leaving site of Damage                                   | Model constant         |
| kass_reas     | 5e-007  | PARP binding to sDSB  | [3]                    |
| kass_reat     | 0.02    | PARP dissociation from sDSB                                   | [3]                    |
| kass_reau     | 0.005   | Recruitment of LiIII/XRCC3 to sDSB                            | [12,13]                |
| kass_reav     | 0.02    | LiIII/XRCC3 leaving site of Damage                            | Model constant         |
| kass_reaw     | 0.00035 | LiIII/XRCC3 binding to DNA-PK-sDSB Complex                    | [12,13]                |
| kass_reax     | 0.0006  | Accurate ligation of sDSB and dismantling of Repair Complex   | [1,14]                 |
| kass_reay     | 0.0009  | Inaccurate ligation of sDSB and dismantling of Repair Complex | [1,14]                 |
| kass_reaz     | 0.6     | Recruitment of PARP to cDSB                                   | [3]                    |
| kass_reba     | 4e-007  | PARP binding to cDSB  | [3]                    |
| kass_rebb     | 0.02    | PARP leaving site of Damage                                   | [3]                    |

|             |        |   |         |
|-------------|--------|---|---------|
| kass_rebc   | 0.005  | Recruitment of LIII/XRCC3 to cDSB                             | [12,13] |
| kass_rebd   | 0.0002 | LIII/XRCC3 binding to DNA-PK-cDSB Complex                     | [12,13] |
| kass_rebe   | 0.0006 | Accurate ligation of cDSB and dismantling of Repair Complex   | [1,14]  |
| kass_rebf   | 0.0009 | Inaccurate ligation of cDSB and dismantling of Repair Complex | [1,14]  |
| kdiss_DNAPK | 0.02   | DNA-PK dissociation from DSB                                  | [3,4]   |

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