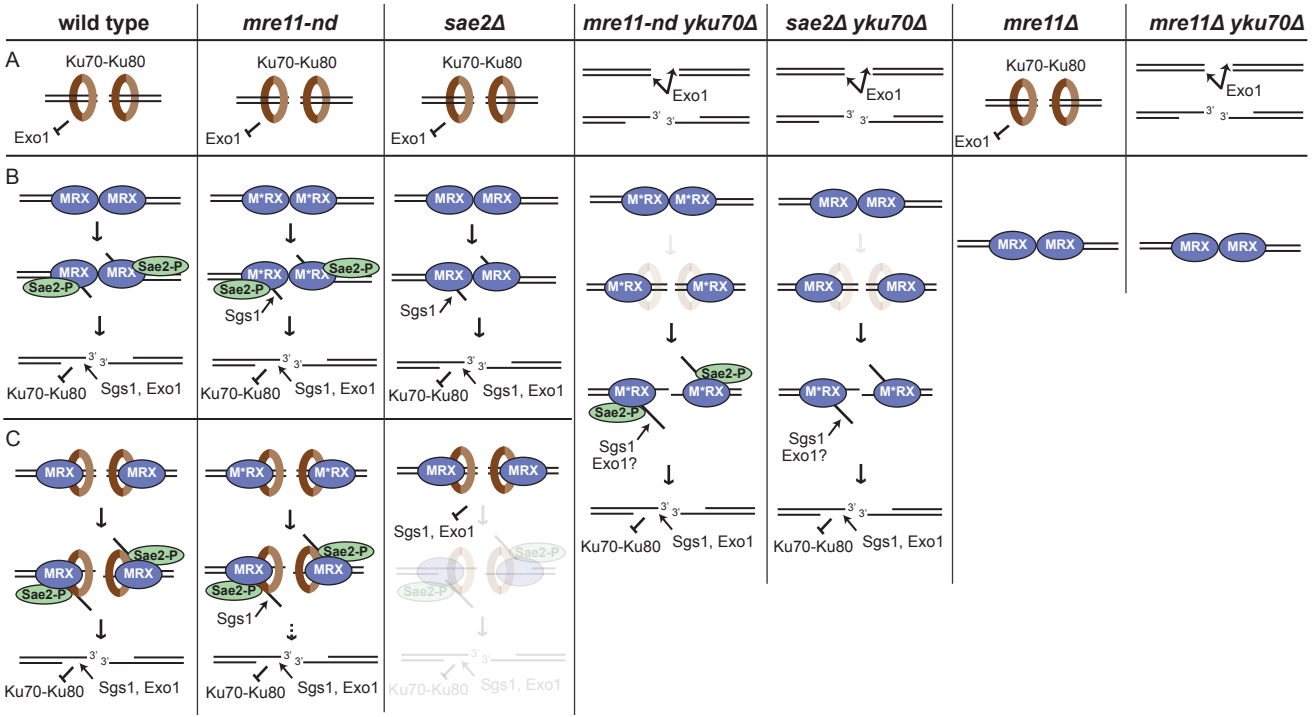

Figure 7: Models for the interplay between resection machinery and Ku at DSB ends. In wild type cells DSBs can exist in three dynamic states: (A) Ku-bound, which blocks access to Exo1, (B) MRX-bound which can initiate end-processing and (C) MRX/Ku-bound, which can initiate NHEJ and removal of Ku is required to allow resection initiation. Recruitement of Sae2 in G2 and clipping of the ends allows access to the processive resection machinery and creates an intermediate that can no longer convert states and commits to HR. In nuclease defective mutants of Mre11, though compromised for initial processing, the presence of Sae2 channels ends to HR and redundant activity from Sgs1-Dna2 allows initiation of resection. In the absence of SAE2, the MRX-bound ends can still initiate resection, presumably with some assistance by Sgs1, whereas the Ku-bound and MRX-Ku-bound ends are blocked. When the end protection by Ku is lost, in *mre11-nd yku70Δ* and *sae2Δ yku70Δ* for example, MRX-naked ends can be resected by Exo1. For the MRX-bound ends even if compromised for the initial clipping, the absence of Ku allows Sgs1 (and maybe Exo1) to assist in initiating resection of the DSB. Finally in the absence of Mre11, where the only state present is the Ku-bound state, access of Exo1 is blocked in a Ku-dependent manner.

TABLE 1. Yeast strains

Strain	Genotype[α]	Source
W1588-4C	*MAT***a**	R. Rothstein
W1588-4A	*MAT*α	R. Rothstein
YHK595-3B	*MAT***a** *rad51::LEU2*	H. Klein
LSY0624	*MAT***a** *exo1::URA3*	(Kirkpatrick et al, 2000)
LSY0779	*MAT***a** *mre11::LEU2*	(Moreau et al, 1999)
LSY0782	*MAT*α *mre11-H125N::URA3::mre11-H125N*	(Moreau et al, 2001)
LSY0785	*MAT***a** *hdf1::HIS3*	This study
LSY0793	*MAT***a** *mre11::LEU2 hdf1::HIS3*	This study
LSY0797	*MAT***a** *mre11-H125N::URA3::mre11-H125N hdf1::HIS3*	This study
LSY0798	*MAT*α *mre11-H125N::URA3::mre11-H125N hdf1::HIS3*	This study
LSY1009	*MAT*α *ade3::GAL1-HO*	This study
LSY1091	*MAT***a** *sae2::KANMX6*	This study
LSY1092	*MAT*α *sae2::KANMX6*	(Mimitou & Symington, 2008)
LSY1199	*MAT*α *dnl4::URA3*	H. Klein
LSY1200-1D	*MAT***a** *rad51::LEU2 hdf1::HIS3*	(Morgan et al, 2002)
LSY1419	*MAT*α *exo1::HIS3 mre11-H125N*	(Lam et al, 2008)
LSY1428	*MAT***a** *mre11::KlURA3 exo1::HIS3*	This study
LSY1475	*MAT***a** *sgs1::HIS3*	This study
LSY1606	*MAT***a** *rad27::TRP1*	This study
LSY1661	*MAT*α *rad55::HIS3 ade2-ISceI*	(Mozlin et al, 2008)
LSY1709-9D	*MAT*α *rad51::LEU2 ade2-n::TRP1::ade2-I lys2::GAL-*	(Mimitou &

	ISCEI	Symington, 2008)
LSY1805-2A	*MAT***a** *sae2::KANMX6 mre11-H125N::URA3::mre11-H125N*	This study
LSY1805-23C	*MAT***a** *sae2::KANMX6 exo1::HIS3*	This study
LSY1879-3B	*MATα rad51::LEU2 exo1::HIS3 mre11-H125N::URA3::mre11-H125N ade2-n::TRP1::ade2-ISceI lys2::GAL-ISCEI*	This study
LSY1880-36A	*MATα rad51::LEU2 mre11-H125N::URA3::mre11-H125N ade2-n::TRP1::ade2-ISceI lys2::GAL-ISCEI*	This study
LSY1975	*MAT***a** *sgs1::HPHMX4*	(Mimitou & Symington, 2008)
LSY2012	*MAT***a** *sgs1::HPHMX4 exo1::HIS3*	(Mimitou & Symington, 2008)
LSY2130	*MAT***a** *mre11-H125N::URA3::mre11-H125N exo1::HIS3 hdf1::LEU2*	This study
LSY2132	*MATα hdf1::LEU2 sae2::KANMX6*	This study
LSY2134	*MATα exo1::HIS3 hdf1::LEU2 sae2::KANMX6*	This study
LSY2146-5D	*MAT***a** *sgs1::HPHMX4 mre11-H125N::URA3::mre11-H125N*	This study
LSY2146-9B	*MAT***a** *sgs1::HPHMX4 mre11-H125N::URA3::mre11-H125N hdf1::HIS3*	This study
LSY2147-4A	*MATα sgs1::HPHMX4 mre11::LEU2*	This study
LSY2147-1C	*MATα sgs1::HPHMX4 mre11::LEU2 hdf1::HIS3*	This study
LSY2156-407D	*MAT***a** *mre11::klURA3 hdf1::LEU2 exo1::HIS3*	This study
LSY2157	*MATα mre11-H125N*	This study
LSY2171-11D	*MAT***a** *rad51::LEU2 sgs1::HPHMX4 mre11-H125N::URA3::mre11-H125N ade2-n::TRP1::ade2-ISceI lys2::GAL-ISCEI*	This study
LSY2171-29A	*MATα rad51::LEU2 sgs1::HPHMX4 hdf1::HIS3 mre11-H125N::URA3::mre11-H125N ade2-n::TRP1::ade2-ISceI lys2::GAL-ISCEI*	This study
LSY2172-24C	*MAT***a** *rad51::LEU2 ade3::GAL1-HO*	This study

LSY2172-17C	*MAT***a** *rad51::LEU2 sgs1::HPHMX4 ade3::GAL1-HO*	This study
LSY2193-16B	*MAT***a** *rad27::TRP1 hdf1::LEU2*	This study
LSY2209-28A	*MAT***a** *sgs1::HPHMX4 exo1::URA3 hdf1::HIS3*	This study
LSY2228-52B	*MAT***a** *rad51::LEU2 sae2::KNMX6 ade3::GAL1-HO*	This study
LSY2228-40C	*MAT***a** *rad51::LEU2 sae2::KNMX6 hdf1::HIS3 ade3::GAL1-HO*	This study
LSY2229-3C	*MAT***a** *sae2::KNMX6 mre11-H125N::URA3::mre11-H125N hdf1::HIS3*	This study
LSY2245-8C	*MAT***a** *sae2::KNMX6 sgs1::HPHMX4 hdf1::HIS3*	This study
LSY2258-12B	*MAT***a** *rad51::LEU2 mre11-H125N::URA3::mre11-H125N hdf1::HIS3 ade3::GAL1-HO*	This study
LSY2265-10D	*MAT***a** *rad51::LEU2 mre11-H125N::URA3::mre11-H125N ade3::GAL1-HO*	This study
LSY2265-8A	*MAT***a** *rad51::LEU2 mre11-H125N::URA3::mre11-H125N sgs1::HPHMX4 ade3::GAL1-HO*	This study
LSY2275-1D	*MAT***a** *sae2::KNMX6 dnl4::URA3*	This study
LSY2299-11B	*MAT***a** *mre11-H125N::URA3::mre11-H125N dnl4::KNMX6*	This study
LSY2305-1C	*MAT***a** *mre11::LEU2 dnl4::KNMX6*	This study

[α] All strains listed are of the W303 genotype (*trp1-1 his3-11,15 can1-100 ura3-1 leu2-3,112 ade2-1*). Only the mating type and differences from this genotype are shown

References:

Kirkpatrick DT, Ferguson JR, Petes TD, Symington LS (2000) Decreased meiotic intergenic recombination and increased meiosis I nondisjunction in *exo1* mutants of *Saccharomyces cerevisiae*. *Genetics* **156:** 1549-1557

Lam AF, Krogh BO, Symington LS (2008) Unique and overlapping functions of the Exo1, Mre11 and Pso2 nucleases in DNA repair. *DNA Repair (Amst)* **7:** 655-662

Mimitou EP, Symington LS (2008) Sae2, Exo1 and Sgs1 collaborate in DNA double-strand break processing. *Nature* **455:** 770-774

Moreau S, Ferguson JR, Symington LS (1999) The nuclease activity of Mre11 is required for meiosis but not for mating type switching, end joining, or telomere maintenance. *Mol Cell Biol* **19:** 556-566

Moreau S, Morgan EA, Symington LS (2001) Overlapping functions of the *Saccharomyces cerevisiae* Mre11, Exo1 and Rad27 nucleases in DNA metabolism. *Genetics* **159:** 1423-1433

Morgan EA, Shah N, Symington LS (2002) The requirement for ATP hydrolysis by *Saccharomyces cerevisiae* Rad51 is bypassed by mating-type heterozygosity or RAD54 in high copy. *Mol Cell Biol* **22:** 6336-6343

Mozlin AM, Fung CW, Symington LS (2008) Role of the *Saccharomyces cerevisiae* Rad51 paralogs in sister chromatid recombination. *Genetics* **178:** 113-126