

# MSH6 Sequence update

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# CFR *hMSH6* Study (2004-2005)

• IHC negative	O	U	H	M	S	A	#tested
• <i>MSH6</i> alone	4	2	0	6	14	7	33
• <i>MLH1/MSH6</i>	0	0	x	1	2	0	3
• <i>MLH1/MSH2/MSH6</i>	0	12	0	0	2	0	14
• <i>MSH2/MSH6</i>	9	8	3	13	16	8	57
• Other (2/6/P2, 6/P2)	0	0	0	0	0	2	2
• MSI-L	16	16	16	16	16	16	96
• MSS (same as <i>MLH1/MSH2</i> project)	52	14	4	17	43	17	147
						Total	351

# Group: MSH6 only

Missense 3 (10%)

- 1193T>A (V398E) (EX4) novel
- 2341C>T (P781S) (EX4) novel
- 320C>T (P107L) (EX2) novel

Nonsense 15 (48%)

- 3514\_3515insA (R1176X)
- 3335\_3336insATGA (I1113X) n=2
- 3078\_3079insT (N1039X)
- 3725\_3737delGTACATTATTTTC (H1248X)
- 1519\_1520insTCCAAGTATGATA (R510X)
- 651\_652insT (K218X)
- 467C>G (S156X)
- 3528\_3532delACTTG (S1185X)
- 10C>T (Q4X)
- 2690\_2691insA (E899X)
- 3987\_3988insGTCA (E1341X)
- 3439-2A>G (splice) n=2
- 3850\_3851insATTA (F1289X)

Negative 13 (42%)

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Total 31

# Group: MSH2/MSH6

Missense: 2 (4%)

- 257C>T (T86I) (EX1) novel
- 3226C>T (R1076C) (EX5) novel

Nonsense: 3 (5%)

- 3514\_3515insA (R1176X)
- 1444C>T (R482X)
- 4071\_4072insGATT (E1359X)  
(novel & also seen in MSS group)

Negative: 50

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55

# Group: MSH6 / other

	MLH1/ MSH6	MLH1/ MSH2/ MSH6	MSH2/ PMS2/ MSH6
Missense	0	0	0
Nonsense	0	0	0
Negative	3	14	1
Total	3	14	1

# Group: MSI-L

Missense: 1

- 1364A>C (N455T) (EX4) novel

Unknown Consequence: 1

- 4083+24\_4083+28delGTTTGA  
(3' UTR deletion)

Negative: 88

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90

# Group: MSS

Missense: 4

- 4070T>C (I1357T) (EX10) novel
- 1526T>C (V509A) (EX4) novel
- 1019T>C (F340S) (EX4) *Int J Cancer* 2000; 85:606
- 229C>T (R77W) (EX1) novel

Unknown Consequence: 4

- 3765\_3766insGAT (D1255\_Y1256insD) (EX8) novel
- 2302\_2304delCCT (P768del) (EX4) novel
- 3438+2\_3438+3insT (IVS5) novel
- 4071\_4072insGATT (E1359X) (EX10) novel

Negative: 128

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# MLPA Analysis

## 2 Positive

del Exon 1 MSH6

MSH2/MSH6 group, 2135\_2136insT in MSH2

del Exon 3 MSH6

MSH6 only group, no other mutation identified

## 340 Negative

## 6 Failures

# Where are we at!!

1. Review and confirm IHC results
2. Review MSI results
3. Confirm MLPA results
4. Incorporate MLH1 and MSH2  
Sequence Results
5. Need to test affected family members
6. Write paper

# What we need from Toronto:

- 1- MSI marker data for all individual markers, 2- and IHC number coding, if possible, AND 3- mutation status for MLH1 and MSH2 (+/- for pathogenic alteration) for following Person\_ID's:  
110031023211, 110031340995, 110030010565, 110030017925, 110030020176,  
110030022453, 110030031694, 110030086342, 110030095152, 110030103121,  
110030000244, 110030010987, 110030107627, 110030080048
- IHC results or “Not tested” for MSS samples  
per Dr. Bapat, IHC slides being reviewed at Toronto
- Relatives of following Person\_ID's:  
110030049332, 110030074660, 110030000244, 110030010987, 110031047533,  
110030083448 (Please include this ID when referring to relative Person\_ID so we know which exon to sequence)

# What we need from USC:

- **1- MSI marker data for all individual markers, 2- and IHC number coding, if possible, AND 3- mutation status for MLH1 and MSH2 (+/- for pathogenic alteration) for following Person\_ID's:**  
123002830009, 125001163045, 125001767011, 124009157009, 125001037003,  
125001839006, 127006012001, 127007246002, 127007633022, 127007994001
- Suspect data entry error for IHC results on following samples, please double-check:  
127006544001, 127006562001, 127006887001, 127007246002, 127007291001,  
127007598001, 127007633001, 127007633022, 127007994001, 127008191001,  
127008281001, 127009712001
- IHC results or “**Not tested**” for **MSS samples**
- Relatives of following Person\_ID's:  
123005837001, 123006908001, 121003039001 (Please include this ID when referring to relative Person\_ID so we know which exon to sequence)

# What we need from Australia:

- MSI marker data OK for ALL
- Want **IHC number coding, if possible** on these Person\_ID's:  
130350052018, 130350059002, 130350166011, 130656012014, 130656049001,  
130151004017, 130350149020, 130151028001, 130350055011, 130350071010,  
130350300012
- Need mutation status for MLH1 and MSH2 (+/- for pathogenic alteration) for following Person\_ID's:  
130350059002, 130350059020, 130151004017, 130350149020, 130350055011,  
130350071010, 130350300012
- IHC results or "**Not tested**" for **MSS samples**
- Relatives of following Person\_ID's:  
130656012014, 139921016001, 130151028001, 130350172001,  
130350195001, 139920245001, 139910311001, 139920029001, (Please include this ID when referring to relative Person\_ID so we know which exon to sequence)

# What we need from Hawaii:

- 1- MSI marker data for all individual markers, 2- and IHC number coding, if possible, AND 3- mutation status for MLH1 and MSH2 (+/- for pathogenic alteration) for following Person\_ID's:  
140000010444 and 140000015861
- IHC results or “Not tested” for MSS samples
- Received 7 relatives on 12/1/05.  
Please send PROBAND PERSON\_ ID associated with each relative Person\_ID so we know which exon to sequence

# What we need from Seattle:

- 1- MSI marker data for all individual markers (all samples)
- 2- Want IHC number coding, if possible (all samples)
- 3- Mutation status for MLH1 and MSH2 (+/- for pathogenic alteration - all samples)
- Relatives of following Person\_ID's:  
160000005750, 160000006057, 160000019114, 160000021706, 160000009706,  
160000012921, 160000004229, 160000014466, (Please include this ID when referring to  
relative Person\_ID so we know which exon to sequence)

# What we need from Mayo:

- 1- MSI marker data for all individual markers, 2- and IHC number coding, if possible, AND 3- mutation status for MLH1 and MSH2 (+/- for pathogenic alteration) for following Person\_ID's:  
150550040004, 150550067003, 150550215005, 150550221004, 150550221012, 150550284015, 150570412001, 150570316017, 150570623012, 150570202003, 150651076001
- Confirm IHC and MSS results for Person\_ID: 150570412001
- Relatives of following Person\_ID's:  
150560314001, 150570132001, 150651076001, and 150570258001 (Please include this ID when referring to relative Person\_ID so we know which exon to sequence. NOTE: we did receive 7 samples in October – not tested yet – Need to know associated proband so we know which exon to sequence)