KIF6 Genotyping Assay

Case Study Examples

Case studies are presented for educational purposes only and are not actual patients. References are listed on the last page of these case studies and are available upon request.
BN’s Story

BN’s physician is concerned because BN’s cholesterol is high and he will not take his prescribed statin therapy.* After discussion with BN, his physician ordered a KIF6 genotyping test to help appraise the potential event reduction benefit from statin therapy. **BN is a KIF6 carrier.**
BN – **KIF6 Carrier**

**Family History**
- Father with CABG (Coronary Artery Bypass Graft), age 63

**Lab Values**
- **Total Cholesterol:** 220 mg/dL
- **LDL-C:** 148 mg/dL
- **HDL-C:** 42 mg/dL
- **Triglycerides:** 149 mg/dL

*KIF6* carriers have either one or two 719Arg alleles. These patients are reported as either Arg/Arg or Trp/Arg and are listed in green in the “Carrier” column.

**Past Medical History**
- 54 year old male with no known history of CAD (Coronary Artery Disease)
- Non-smoker
- Dyslipidemia – declined statin therapy because he has heard about side effects from statins
- Hypertension – on treatment; well-controlled
- **BMI:** 28

<table>
<thead>
<tr>
<th>Test Performed</th>
<th>Noncarrier</th>
<th>Carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>KIF6 Genotyping Assay</td>
<td>Trp/Arg</td>
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</tr>
<tr>
<td>(KIF6 719 Genotype)</td>
<td></td>
<td>t/c</td>
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| Single Nucleotide Polymorphism = rs20455 |

**What does this mean?**
- In recent studies, patients with the *KIF6* 719Arginine gene variant (*KIF6* carriers) had significantly increased risk of a CHD event,** independent of traditional risk factors such as LDL-C levels***1–4,6
- Statin therapy was shown to reduce events more effectively in *KIF6* carriers than in noncarriers, despite similar reductions in LDL-C levels1,5,6

**Clinical Lessons**
1) Since BN is a *KIF6* carrier, he may have elevated risk for CHD, independent of his LDL-C levels.
2) BN also has traditional risk factors for heart disease.
3) BN and his physician now have more knowledge about the potential benefit of statin therapy for BN.
4) BN’s physician may suggest *KIF6* genotyping for BN’s first degree relatives.

*Since BN is a *KIF6* carrier, he may have an additional reason beyond his elevated LDL-C to take his prescribed statin medication*

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*To date, the benefit of statin therapy for *KIF6* carriers has only been studied with atorvastatin and pravastatin.
** In published studies about *KIF6*, CHD events include but were not limited to heart attack, stroke and plaque build up in arteries requiring stent replacement.
*** Study populations predominantly consisted of Caucasians 45 years of age and older.
JP’s Story

JP’s physician is concerned because JP continues to gain weight and has a poor diet. To learn more about JP’s additional risk for CHD events, his physician ordered KIF6 genotype testing. **JP is a KIF6 non-carrier.**
**JP – KIF6 Noncarrier**

### Family History
- Premature heart disease

### Lab Values
- **Total Cholesterol:** 203 mg/dL
- **LDL-C:** 125 mg/dL
- **HDL-C:** 38 mg/dL
- **Triglycerides:** 202 mg/dL

### Past Medical History
- 47 year old male
- Non-smoker
- Dyslipidemia
- Insulin resistance
- **BMI:** 30

### KIF6 Genotyping Assay (KIF6 719 Genotype)
- **Noncarrier**
- **Carrier**

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**What does this mean?**

- **KIF6** noncarriers have less risk of CHD events* than **KIF6** carriers, according to recent research**1–4
- When compared to **KIF6** carriers, noncarriers have less CHD event reduction with statin therapy***1,5,6

### Clinical Lessons

1) According to European Guidelines for Cardiovascular Heart Disease guidelines, JP has elevated risk for heart disease from traditional risk factors including elevated triglycerides and low HDL-C.7
2) The **KIF6** carrier genotype is an independent risk factor for CHD but since JP is a noncarrier, it is not a risk factor for him.
3) JP’s physician may focus on risk factors other than **KIF6**.
4) Since JP is a noncarrier, and has a family history of premature CHD along with low HDL-C and elevated triglycerides, his physician may consider therapies in addition to statins.

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In addition to statin therapy, JP’s physician may want to consider adding a non-statin to his treatment plan

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* In published studies about **KIF6**, CHD events include but were not limited to heart attack, stroke and plaque build up in arteries requiring stent replacement.
** Study populations predominantly consisted of Caucasians 45 years of age and older.
*** To date, the benefit of statin therapy for **KIF6** carriers has only been studied with atorvastatin and pravastatin.
BR’s Story

BR is concerned about her risk for heart disease because of her family history. Her neighbor is taking statin therapy and she wants to know if she needs a statin. In order to better understand her risk for CHD events, her physician ordered \textit{KIF6} genotype testing. \textit{BR is a KIF6 noncarrier}. 
BR – *KIF6* Noncarrier

**Family History**
- Father – MI (Myocardial Infarction), age 55, deceased
- Mother – Stroke, age 82, deceased

**Lab Values**
- **Total Cholesterol:** 201 mg/dL
- **LDL-C:** 122 mg/dL
- **HDL-C:** 48 mg/dL
- **Triglycerides:** 165 mg/dL

*KIF6* noncarriers lack the 719Arg allele. These patients have two Trp alleles (Trp/Trp) and are listed in purple in the “Noncarrier” column.

**Past Medical History**
- 48 year old female
- Non-smoker
- BMI: 27

**Clinical Lessons**
1) The *KIF6* carrier genotype is an independent risk factor for CHD but since BR is a noncarrier, it is not a risk factor for her.
2) BR’s physician may focus on risk factors other than *KIF6*.
3) BR has a family history of heart disease so her physician may wish to test for other genetically-linked CHD risk factors.
4) If BR’s physician decides to treat her with medication, he may want to consider therapies in addition to statins.

Since BR is a *KIF6* noncarrier, she may be motivated to adhere to a healthy lifestyle to lower her CHD event risk

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** Study populations predominantly consisted of Caucasians 45 years of age and older.
*** To date, the benefit of statin therapy for *KIF6* carriers has only been studied with atorvastatin and pravastatin.
PR’s Story

Since PR had an ACS (Acute Coronary Syndrome), he may benefit from statin therapy. If PR is a \textit{KIF6} carrier, the analysis of the PROVE IT-TIMI 22 trial of ACS patients suggests that he may benefit from intensive statin therapy. In this study, \textit{KIF6} noncarriers received no additional event reduction from intensive versus moderate statin treatment (Fig. 1).\textsuperscript{15}
PR – *KIF6* Carrier

**Family History**

- Father with early MI (Myocardial Infarction), age 54

**Lab Values**

- **Total Cholesterol:** 177 mg/dL
- **LDL-C:** 106 mg/dL
- **HDL-C:** 44 mg/dL
- **Triglycerides:** 135 mg/dL

*KIF6* carriers have either one or two 719Arg alleles. These patients are reported as either Arg/Arg or Trp/Arg and are listed in orange in the “Carrier” column.

**Past Medical History**

- 52 year old male
- Smokes 2 packs per day
- ACS (Acute Coronary Syndrome) 30 days ago
- BMI: 28

In order to learn more about PR’s probable risk reduction from intensive statin therapy, his doctor tests him for the *KIF6* genotype. **PR is a *KIF6* carrier.**
What does this mean?

- Intensive statin therapy was found to reduce events more effectively than standard dose therapy in KIF6 carrier in the PROVE IT-TIMI 22 trial of ACS patients.
- KIF6 carriers in PROVE IT-TIMI 22 also had significant event reduction as early as 30 days (Fig. 2).

FIGURE 2: TIME TO BENEFIT IN PROVE IT-TIMI 22
According to KIF6 719Arg Carrier Status

Clinical Lessons

1) PR should quit smoking to improve his heart health.
2) PR was hospitalized with an ACS and since he is a KIF6 carrier, he may be more likely to benefit from intensive statin therapy.
3) Since PR and his father had premature heart disease, PR’s physician may suggest screening first degree relatives for the KIF6 genotype.

PR’s KIF6 genotype indicates that he may have greater event reduction from intensive versus standard dose statin therapy.

* To date, the benefit of statin therapy for KIF6 carriers has only been studied with atorvastatin and pravastatin. In the PROVE IT-TIMI 22 study, intensive and standard dose statin therapy were studied with 80 mg atorvastatin and 40 mg pravastatin, respectively.


(4) Shiffman, D, et al. A Kinesin Family Member 6 Variant Is Associated With Coronary Heart Disease in the Women’s Health Study. JACC. 2008; 51(4): 444-448.


(8) www.statincheck.com/what_clinical.php 24.08.2010

The KIF6 Genotyping Assay was developed by Celera and is now CE marked and approved for sale and distribution within the EU.

Case studies are presented for educational purposes only and are not actual patients. The information and data presented in these case studies are based on study populations of predominantly Caucasian men and women over 45 years old.