



**SCRIPT DOCTOR: MEDICINE IN THE MEDIA**

# Quick Comment on *House* about Duke Vaccine Trial Provokes Public Response Bigger than *CBS Evening News*' Mention

By Andrew Holtz, MPH

The episode of *House* that aired on Tuesday, March 6 included suspicions that the main character, Dr. Gregory House, might have a brain tumor that could not be successfully treated by conventional therapies. At about 9:33 pm (8:33 pm central and mountain time) the character of Dr. Robert Chase said, "They've got another trial going on at Duke. Fifteen percent extend their lives beyond five years. If you are positive for protein PHF..."

*"Who knew that anyone was listening to the show that carefully? I mean, honestly, the thing went by in like three seconds."*

about it. Colleagues and friends called and e-mailed their congratulations that his work was recognized on a hugely popular TV show. Patients and their families wanted to know if they could get the treatment.

"That often happens—even though it was mentioned in a fictional setting, people suddenly think, 'Well, maybe there's something out there that I don't know about, and it's important. So they do start calling up,'" said Henry Friedman, MD, Deputy Director of the Preston Robert Tisch Brain Tumor Center at Duke. He says the primetime plug made them look good to patients and the institution.

"And my kids thought this was way cool," Dr. Friedman said. That's because that episode's guest star was their favorite musician, Dave Matthews.

The higher-ups at Duke were pleased with the surprise attention.

"I was delighted. People all over the country were e-mailing us," says Henry Friedman, MD, Deputy Director of the Preston Robert Tisch Brain Tumor Center at Duke. He says the primetime plug made them look good to patients and the institution.

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## How Did the Mention Come About?

But Dr. Friedman had no idea what prompted the mention of Duke brain cancer research, so he called *House* writer Lawrence Kaplow with thanks and a question.

"Why'd you say [Duke]? Especially us over Harvard?" Dr. Friedman asked.

From his end of the conversation, Kaplow recalls Dr. Friedman mentioning the Tisch family, which donated several million dollars to Duke after New York businessman Preston Robert

Tisch was treated there. The family also has strong TV connections: Preston Robert's brother, Laurence, once ran CBS.

"It was so funny," the *House* writer said about his call with Dr. Friedman. "He was like, 'Thank you so much for mentioning Duke, we're talking to the Chairman of Fox, we're very close with the Tisch family, and obviously Fox has a relationship with Tisch. And it was so nice of Fox to mention Duke.'"

Kaplow then told him the real source of the line: "And I'm like, 'Fox?! Tisch?! No! It's my friend Michael!'"

Kaplow's friend was treated at Duke.

"He had a Grade IV glioblastoma]. He was told at three places that he was gonna die."

"I was touched that [Friedman] took the time to call up and say thank you. I said there's no 'thank you' necessary. It was just a 'shout out' that my friend, who is still alive, would get a kick out of," Kaplow said.

## 'No Product Placement'

He said the mention of Duke was not any kind of "product placement," which he says they carefully avoid in any case. As the storyline involving



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brain cancer developed, he just wanted to toss in a casual reference to his friend's brain tumor experience.

"That's why, when I was researching, I just threw into a Google search 'What's Duke doing now?' You know, give me something crazy that they are doing now. I found one and I mentioned it," he said.

But in addition to his friend, there were 24 million other viewers watching that episode—some of them with powerful personal reasons to read more than was intended into the mention of Duke's research.

"In general when patients call, they think we are sort of right around the corner from the breakthrough and the cure. And really that's not the way it's going to happen; it's going to be slow incremental advances," Dr. Sampson says.

## Starting Phase III Trials

He said he is confident the therapeutic cancer vaccine they are working on will lead to new treatment options for some patients, but it's only now entering Phase III trials.

The approach attempts to stimulate an immune system assault on tumor cells with injections of a variant of epidermal growth factor receptor protein. The variant, known as EGFRvIII, is present in about a third of glioblastoma tumors. Celldex Therapeutics has licensed the vaccine and is currently enrolling patients who have tumors expressing EGFRvIII.

Even though the therapy is not quite ready for primetime, so to speak, it has been getting a good bit of attention in the news media. Dr. Sampson says he pre-

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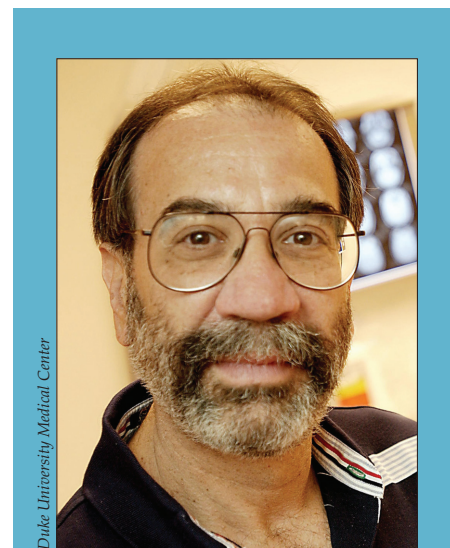
Duke University Medical Center

John H. Sampson, MD, PhD, hadn't seen the episode of *House* that mentioned his vaccine study when it first aired, but, boy, did he hear about it! Colleagues and friends called and e-mailed their congratulations that his work was recognized on a hugely popular TV show. Patients and their families wanted to know if they could get the treatment.

Before he could finish the sentence, Dr. House cut him short. The brief remark was barely six seconds long. It didn't mention a specific therapy. But the character did say "Duke."

"The next morning people started calling up and saying, 'They mentioned your vaccine study on *House*,'" recalled John H. Sampson, MD, PhD, Associate Professor of Surgery and Assistant Professor of Pathology at Duke Comprehensive Cancer Center. "Actually they didn't specifically say it was a vaccine, but I guess that's what the majority of people took it to mean."

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Henry Friedman, MD, Deputy Director of Duke's Brain Tumor Center: "I was delighted. People all over the country were e-mailing us—And my kids thought this was way cool, because that episode's guest star was their favorite musician, Dave Matthews."

## FDA Approval for Fragmin to Reduce Recurrence of Blood Clots in Cancer Patients

The FDA has approved a new indication for dalteparin (Fragmin) for the extended treatment of symptomatic venous thromboembolism (VTE) to reduce the recurrence of the problem in patients with cancer. The drug is the first low-molecular-weight heparin approved in the US for the extended treatment of recurrent VTE in patients with cancer. The condition of VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE).

"Cancer treatments and the disease itself put this patient population at significantly higher risk than non-cancer patients for developing DVT and PE," Frederick Rickles, MD, Clinical Professor of Medicine at George Washington University Medical Center, said in a news release. The approval was based on data from the CLOT study, which evaluated the safety and efficacy of dalteparin in reducing the recurrence of DVT/PE in patients with cancer, compared with an oral anticoagulant. The CLOT study showed that, during a six-month period, nearly twice as many patients (53) treated with warfarin had

at least one episode of DVT or PE compared with patients treated with once-daily dalteparin (27 patients), with most of the difference occurring during the first month of treatment. The benefit was maintained over the six-month study period. Mortality rates were similar between the study groups at the end of the study.

"The CLOT study provides clinical evidence that Fragmin is more effective than traditional oral anticoagulant therapy in reducing risk of recurrent VTE in patients with cancer," Dr. Rickles said.

The drug had already been approved for prevention of DVT, which may lead to PE, in patients undergoing

hip-replacement surgery, in at-risk patients undergoing abdominal surgery and in at-risk acutely ill patients whose mobility is severely restricted. Fragmin is also approved for prophylaxis of ischemic complications resulting from unstable angina and non-Q-wave myocardial infarction when used with aspirin.

### ScriptDoctor

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fers to see work like his pop up in entertainment shows like *House*.

"It's really terrific. And let me tell you one of the good things about it: Sometimes, when you are on a show, you get interviewed or something like that, it can often be as negative for you personally as it is positive. Sometimes it causes jealousy, or maybe you get misquoted. But something like what happened with *House* is really in essence out of our control, we can't really be misquoted because we aren't really being quoted—it's just a fictional story."

The EGFRvIII vaccine has also been featured in *Newsweek*, and in March it was highlighted by Katie Couric on the *CBS Evening News*.

"That was sort of the biggest thing of late," Dr. Sampson said. "That story created quite a stir as well, but really about equal to the *House* story, if not less."

So a vague reference on *House* that didn't even mention the treatment by name got as much of a response as a series on the evening news that included interviews with him and others involved in the clinical trials? "Yeah, I would say so," Dr. Sampson said.

Even Kaplow, who started the whole thing with his "shout out" to a friend, was amazed by the impact at Duke.

"Who knew that anyone was listening to the show that carefully? I mean, honestly, the thing went by in like three seconds," he said.

## Breaking the Complex Code of Tumor Resistance Mechanisms

Tumor resistance to cytotoxic drugs can occur at the start of therapy (known as intrinsic resistance), as early as the first treatment or over time after an initial period of tumor response (acquired resistance).<sup>1</sup>

The mechanisms that cause intrinsic and acquired resistance are diverse. Below are examples of some of the more common tumor resistance mechanisms.

**Efflux pumps:** Responsible for transporting drugs out of the tumor cell, efflux pumps alter intracellular drug concentrations. Examples are P-glycoprotein or P-gp and the multidrug resistance proteins, MRP1-7.<sup>2</sup>

**Regulation of apoptosis:** Tumor cells can evade signals that normally lead to apoptosis, conferring a survival advantage by making the cell resistant to apoptotic death. An example is the decreased cell surface expression of the Fas death receptor.<sup>3</sup>

**Drug detoxification:** Certain enzymes in the tumor cell play an important role in the cell's defense against invading foreign toxins. For example, glutathione S-transferase, or GST, works synergistically with the efflux pump MRP1 to expel drugs from the cell.<sup>4</sup>

**Drug sequestration:** Drugs can be trapped in special cellular compartments, keeping them away from their site of action. An example is the sequestration of an agent within cytoplasmic organelles.<sup>5</sup>

**Drug target alteration:** Alterations at the drug target site may impair binding. For example, variation in microtubule composition has been associated with tumor resistance.<sup>6,7</sup>

**Damage repair:** Special enzymes within the tumor cell can identify and correct damage to the DNA molecules that encode its genome. For example, overexpression of the enzyme ERCC1 leads to increased DNA repair of drug-induced lesions and diminished response to apoptotic signaling.<sup>8,9</sup>

In order to overcome intrinsic and acquired resistance, new anti-neoplastic agents that can address mechanisms of resistance and demonstrate activity against tumors are needed.

*At Bristol-Myers Squibb, we are currently investigating new agents that may help break the code of intrinsic and acquired tumor resistance and help physicians impact multiple forms of cancer.*

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